

Women's decision making process
regarding prenatal diagnostic testing

Tzafettas, M.

PhD

London Metropolitan University

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Marilena Tzafettas

PhD

London Metropolitan University

In collaboration with King's College Hospital

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Abstract

Objective: Expanding the original scope of the study, which was to explore the decision-making process of pregnant women in the uptake of invasive diagnostic tests - amniocentesis and Chorionic Villus Sampling (CVS) – and taking into account the latest emergence of a Non-invasive Prenatal Testing, NIPT, the primary goal of this study was to explore factors that influence women's decision to have an invasive, a non-invasive or no further testing at all.

Design and sample: The Prenatal Decision Making Questionnaire (PDMQ) developed for the purposes of this study. Following a pilot test and factor analysis, it was distributed to a population of pregnant women (N=421) prior to them receiving their combined screening results. The total sample was divided into three sub-groups according to their risk status (low-intermediate-high) for the analysis.

Results. Logistic regression analysis using the R version 3.0.3 revealed that none of the PDMQ factors had a significant impact on women's decision to have an invasive test (CVS), whereas the following three factors had a significant impact on the decision to have a non-invasive test (NIPT): negative attitude to doctors and an internal locus of control were associated with the uptake of NIPT, whereas a negative attitude to medicine was associated with rejection of NIPT. When risk status was included in the model it was found that uptake of NIPT was predicted by the presence of some level of risk for T21 or T13/T18. On the contrary, uptake of CVS was only predicted by an increased risk for T21.

Conclusion(s): Women's decision making process in prenatal diagnosis is affected by several factors with personalised risk being one of the key determinants. The findings of this study can be used by healthcare professionals in providing the appropriate support and information and facilitating an informed decision during this stage of pregnancy.

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1. Chapter One: Literature Review

1.1. Prenatal diagnosis in the UK

An estimated 7.9 million infants are born each year across the world with a serious birth defect which is defined as “*an abnormality of structure or function, which is present from birth and is life-threatening or has potential to result in disability*” (WHO, 2006, p.1). Even though birth defects are a global issue, they are particularly severe in middle- and low-income countries where 95% of such births occur. More specifically, approximately 3.3 million children under the age of five die from serious genetic birth defects each year, and an equivalent number of those who survive may experience lifelong mental, physical, auditory and visual disabilities, causing a harsh human and economic toll on those affected, their families, and their communities (Howson & Modell, 2008).

However, it is estimated that medical genetic services may contribute to as many as 70% of birth defects being prevented or treated effectively (Christianson, Howson, & Modell, 2006). Nevertheless, even though care can be cost-effective for some conditions such as certain cardiac defects and cleft lip and palate which can be diagnosed and surgically treated, they can also prove to be very expensive, especially for disorders that require long-term treatment such as the treatment of thalassaemia. For such cases, and for countries where needs and resources allow, it is important to emphasise on a combination of care and prevention which includes genetic counselling, prenatal diagnosis and the establishment of services for risk identification and management (Weatherall, Akinyanju, Fucharoen, Olivieri & Musgrove, 2006). This mostly relates to prevention strategies that can be adopted for high risk populations during family planning. For example, in the case of populations at high risk for thalassemia both parents can be genetically screened before conception to identify whether they are carriers of the gene and if so proceed with a pre-implantation genetic diagnosis (PGT) whereby the embryos created in vitro are screened for the respective condition and only those free of it are replaced into the womb via the method of IVF (Sermon, Van Steirteghem, & Liebaers, 2004). This would ensure a normal pregnancy and a healthy baby being born. It is also likely that some individuals in this category will still prefer to fall naturally pregnant regardless of the high risk of passing on the condition to the foetus. Relevant support and resources should be made available in order to support these families throughout their pregnancy and after the delivery of their baby.

What is more, as a result of the social, psychological and economic consequences of caring for children with chromosomal or other birth defects, most pregnant women who have given birth to at least one child with such defects would like to receive reassurance about their unborn foetus's health (Alfirevic & Walkinshaw, 2010). Access, therefore, to safe, accurate and affordable preventive (screening) and diagnostic methods early on in pregnancy, which provide the option of terminating an affected pregnancy or preparing for the birth of a child with health problems, is of paramount importance.

1.2. **Current clinical practice in the UK and latest medical advancements**

At this point it is important to differentiate between prenatal diagnosis and routine antenatal screening. The National Institute for Health and Clinical Excellence (NICE, 2008), the UK National Screening Committee (UK NSC), and the Royal College of Obstetrics and Gynaecology (RCOG – Greentop guideline No. 8, 2008), have set the standards for antenatal care in the UK, recommending that all pregnant women, regardless of age, should be offered routine screening tests between 10 and 20 weeks of gestation. A similar view is held by the American College of Obstetricians and Gynaecologists (ACOG), which suggests that all women – regardless of their age - presenting for antenatal care prior to 20 weeks of gestation should be offered screening tests for foetal aneuploidy (ACOG, 2007).

These screening tests consist of a number of different strategies for the detection of pregnancies at high risk of foetal chromosomal abnormalities, with current methods taking into consideration maternal age, ultrasound findings and maternal serum biochemistry in the first and second trimester of pregnancy (Nicolaidis, 2003).

The availability of non-invasive prenatal methods for the diagnosis of Down's syndrome, for example, is expected to limit the number of cases that will require further invasive diagnostic tests; this is especially true in the case of women over the age of 35, to whom both invasive and non-invasive methods are typically offered. Pregnant women with a specific indication for further testing must receive appropriate genetic counselling regarding the various methods available to them, together with their pros and cons, in order to be in a position to make an informed choice and provide written consent for this.

Current practices in the NHS see all pregnant women being offered a first trimester screening test combining maternal age, sonographic measurement of the foetal nuchal translucency and measurement of maternal serum screening markers (Nicolaidis, 2004; Norton, Brar, & Weiss, 2012). While these methods have improved significantly over the years they are associated with 90-95% detection rates and also have false-positive rates of 2-3% and false-negative of $\geq 5\%$ respectively (Sparks, Struble, Wang, Song, & Oliphant, 2012). Based on the results of this combined test, women identified as being at high risk for carrying a baby with a chromosomal abnormality are offered invasive diagnostic testing in the form of either amniocentesis or Chorionic Villus Sampling (CVS). Whilst these latter procedures are highly accurate (nearing 100% detection rates) they are expensive and also entail a risk of miscarriage (1%) (Sundberg et al., 1997).

In an attempt to address these limitations, and following years of medical research and trials a new test, non-invasive prenatal test (NIPT), has been put forward and has high levels of sensitivity and specificity (Yagel, 2013). This procedure is a blood test and aims to determine the chromosomal status of the foetus through the analysis of cell free foetal DNA (cffDNA) that is located in the maternal circulation (RCOG: Royal College of Obstetricians and Gynaecologists, 2014). While this test is mostly available in the private sector, it also started

being offered at the research site of this study as part of a trial midway our study and therefore our research scope (originally aiming to explore the decision making process regarding invasive diagnostic tests only) was expanded to include this latest medical advancement and assess its impact on women's decision making process regarding prenatal testing.

It is important to note here that with the introduction of Harmony into clinical practice, women are no longer classified as high ($>1:300$) or low ($<1:300$) risk but an intermediate risk group has also been introduced. Therefore, based on their first trimester combined screening results, women are subsequently classified as high ($>1:100$), intermediate ($>1:2500$), or low ($<1:2500$) risk. Those in the high-risk group are then offered the option of either an invasive test (CVS or amniocentesis) or NIPT, while those in the intermediate risk group are only offered the option of NIPT. Women falling in the low risk group are not offered any further testing.

1.3. Screening options offered to pregnant women

The screening options offered to all pregnant women presenting for antenatal care are described below (also illustrated in Table 1.1):

1.3.1. The first trimester combined screening test (11 to 14 weeks of gestation)

The first trimester screening test combines maternal blood serological markers with an ultrasound foetal assessment, in order to estimate the risk of having a specific chromosomal abnormality and, in particular, trisomy 21 (Down's syndrome) or trisomy 18 (Locock, Field, McPherson, & Boyd, 2008). Part of this test (Nuchal Translucency - NT) can additionally help detect other major foetal malformations such as cardiac defects, but does not contribute to the diagnosis of spina bifida.

This type of preventive prenatal testing was up until recently considered to be the most accurate non-invasive method for prenatal detection of either of the aforementioned abnormalities. The accuracy of this method is 86-90%, with a false positive rate of less than 3-5%. It is important to note, however, that a positive result does not necessarily mean the presence of one of these pathologies in the foetus but rather raises attention for further investigation to confirm or disconfirm the disorder.

What is more, the first trimester screening test determines the level of risk based on ultrasound findings (nuchal translucency) and maternal blood biochemical markers, in conjunction with the mother's age (Kirkham, Harris, & Grzybowski, 2005). Because this test is carried out relatively early on in pregnancy, a positive result offers women the opportunity to choose between a diagnostic method such as Chorionic Villus Sampling (CVS) in the first trimester or amniocentesis in the second trimester of the pregnancy (see Table 1.3), and NIPT (if available at the given clinical practice) that is not diagnostic but can provide a more accurate likelihood ration that can act as an intermediate step prior to an invasive procedure being performed or can act as a standalone informative test for those not wishing to engage in invasive testing.

Specifically, the first trimester screening test includes:

- a) *An ultrasound examination with a main emphasis on measuring the foetus's nuchal translucency: a thickening of the skin around the neck (subcutaneous fluid collection) is associated with DS (trisomy 21) (Kirkham et al, 2005).*

The ultrasonographic examination of the first trimester, which was established in 1995, along with that of the second trimester, assists in the identification of morphological (structural) and chromosomal foetal abnormalities such as anencephaly, spina bifida, trisomy 21 (Down's syndrome), trisomy 13 (Patau syndrome), trisomy 18 (Edward's syndrome), etc. Specifically, for the detection of Down's syndrome and other chromosomal abnormalities, there are a number of sonographic markers suggestive of further investigation, such as structural abnormalities of the face, heart and hands of the foetus, chorionic plexus cysts, increased nuchal translucency, short humerus and femur, abnormally increased echogenicity of the bowel, kidney pyelectasia, hypoplastic phalanx of the fifth finger, echogenic intracardiac focus (endocardiac spot), as well as absence of nasal bone, abnormal angle of mandible, widened iliac wing angle etc. (Ilgin-Ruhi, Yurur-Kutlay, Tukun & Bokesoy, 2005).

- b) *Maternal serum markers with the main purpose of diagnosing Down's syndrome (DS) (Locock et al, 2008) as well as other chromosomal abnormalities.*

These maternal serum markers include two hormones related to pregnancy and more specifically to the placenta: the human Chorionic Gonadotrophin (hCG) and the Pregnancy Associated Placenta Protein-A (PAPP-A).

This examination should not be confused with the triple or quadruple test which are carried out between the 15th and 20th weeks of gestation and are less reliable. The first involve the levels of A-foetal protein (commonly known as Alpha-Fetoprotein: AFP), human chorionic gonadotropin (hCG) and unconjugated estriol (UE3) (Kirkham et al, 2005). A reduced amount of AFP and UE3, combined with elevated hCG levels, is usually indicative of an increased risk of DS (Ilgin-Ruhi et al, 2005). In contrast, elevated AFP levels in maternal blood are associated with open lesions of the central nervous system (CNS), such as spina bifida, anencephaly, meningomyelocele, etc. However, abnormal results may be due to testing in the incorrect week of gestation.

AFP is a protein produced by the foetus, while hCG is produced by the placenta and estriol by both the foetus and the placenta (Reis, D'Antona & Petraglia, 2002). The triple test is a non-invasive method with no risk to the mother and / or the foetus. The same applies to the Quadruple test which additionally includes the hormone "Inhibin A".

Table 1.1

Screening Options for Antenatal Testing

Test	Timing (Weeks)	Detection Rate Of Down's Syndrome (%)	False- Positive Rate (%)
First Trimester			
Nuchal Translucency (NT)	10-4/7 to 13-6/7	70 to 71	3.5 to 5
hCG and PAPP-A	10 to 12	53 to 58	5
Combined Test (NT, PAPP-A, hCG, MA)	11 to 14	86 to 90	Less than 3 to 5
NIPT	10 (and over)	99%	Less than 1%
Second Trimester			
Triple Screen (hCG, maternal serum AFP, unconjugated estriol)	15 to 20	60 to 69	5
Quadruple Screen (hCG, inhibin A, maternal serum AFP, unconjugated estriol)	15 to 20	67 to 81 (up to 90 with ultrasonography)	Less than 3 to 5
Ultrasonography	18 to 22	35 to 79	6.7
First and second trimester			
Integrated serum screening (PAPP-A with NT)	11 to 14 and 15 to 20	94 to 96	Less than 3 to 5
Integrated serum screening (PAPP-A without NT)	11 to 14 and 15 to 20	85 to 88	Less than 3 to 5
PAPP-A: Pregnancy Associated Plasma Protein –A; MA: Maternal Age; NT: Nuchal Translucency; hCG: Human Chorionic Gonadotropin; NIPT: Non-invasive prenatal test; AFP: Alpha-fetoprotein			

1.3.2. Non-invasive Prenatal Testing (NIPT)

NIPT is a blood test that enables the testing of the foetus for aneuploidy through cell-free foetal DNA that is extracted from maternal plasma (Skirton & Jackson, 2015).

1.3.2.1. Evidence for effectiveness and strengths of NIPT

Most studies thus far have been conducted on a number of high-risk cohorts (Ashoor, Syngelaki, Wagner, Birdir, & Nicolaides, 2012) and indicate a detection rate for trisomy 21 (T21) (Down Syndrome) of >99% and a false positive rate of approximately <1% (Menezes, Meagher, & Da Silva Costa, 2013). Marginally lower detection rates have been reported for trisomy 18

(T18) (Edward's Syndrome) and even though initially the performance of this test for the detection of trisomy 13 (T13) (Patau's Syndrome) was less reliable, this has been evolving with better results being reported all the time (RCOG, 2014). Detection rates for each of these conditions are illustrated in Table 1.2. It is important to note that while this is still under investigation and trials on populations attending routine first trimester aneuploidy screening are still under way, recent evidence is encouraging in that the accuracy of NIPT obtained for high risk populations is also transferrable to the general population (Nicolaidis, Syngelaki, Ashoor, Birdir, & Touzet, 2012).

Table 1.2

NIPT detection and false-positive rates for each of the three main chromosomal abnormalities tested

	Detection Rate	False-positive Rate
Trisomy 21	>99%	<1%
Trisomy 18	96%	<1%
Trisomy 13	92%	<1%

Note. From Gil, Giunta, Macalli, Poon, & Nicolaidis, 2014.

a) Early performance of the test

A key advantage of NIPT is the very early gestational age at which it can be performed, with foetal genetic material being detectable in the maternal blood as early as 4-5 weeks of gestation (Yagel, 2013). On the contrary, the widely available combined screening tests that have mostly been used to this day include an initial maternal blood serum screen and ultrasound between the 10th and 14th week of gestation, followed by a second serum screen between the 15th and 20th week of gestation-triple test (Rosen & D'Alton, 2005). Women who are identified as being at high risk are then offered the option of CVS at 10-13 weeks or amniocentesis at 15-20 weeks of gestation. Therefore, in favour of NIPT it has been suggested that the early detection of trisomy without the associated risk of miscarriage could help reduce the anxiety in many pregnant women whether this be in the form of offering them reassurance or in terms of providing them with more time to consider their options regarding further testing and subsequent actions (Ravitsky, 2009).

b) Reduction in the number of healthy fetuses lost due to procedural-related complications

When the combined test first came out, it helped reduce the amount of invasive diagnostic procedures carried out and consequently the associated financial expenses and procedural related miscarriages (Yagel, 2013). Therefore, NIPT is expected to contribute further towards this direction.

Due to its high specificity and sensitivity compared to the combined test which has so far been the recommended screening method in the NHS, and if it is incorporated into first-trimester screening procedures, NIPT is most likely going to further reduce the number of women who are referred on for invasive diagnostic testing (Yagel, 2013). This will consequently be reflected in the amount of screen-positive healthy fetuses that are saved and is probably one of the strongest benefits of this new test.

c) Important source of information for all groups of parents

Given that the NIPT does not entail any risk of miscarriage, it offers the opportunity to even those who would avoid an invasive test out of fear of a procedure-related loss, to find out whether their baby suffers from any chromosomal abnormality and thus equip them with more information that may be crucial in their decisions thereafter. Such people will most probably be those who would not consider terminating their pregnancy regardless of the result so would not be willing to take the risk of an invasive test. However, the NIPT can offer them reassurance over their baby's health or even if it indicates a very high possibility of Trisomy 13, 18, or 21 it can help them prepare for the birth of their child and seek all the support and resources they need to help them through. While on the one hand this may, at present, undoubtedly place more financial and resource demands on perinatal clinics, as more women will be continuing with their pregnancy being aware of their baby's condition, on the other it may alleviate much of these women's stress by helping them prepare for the upbringing of their child and feeling supported in doing so (Menezes et al, 2013).

1.3.2.2. Limitations of NIPT

d) Not a diagnostic test

Despite the encouraging evidence so far, the overall sensitivities and specificities for NIPT are so far >95% with false-positive rates of <1% (Yagel, 2013). This means that while it is a test with high sensitivity it still does not provide a definitive result and therefore should not be used as a replacement for invasive testing in high-risk populations. It should instead be treated as a new higher-performance screening test for T21, T18, and T13 which identifies those at high-risk who should then be referred on for invasive diagnostic testing (amniocentesis or CVS) in order to verify the results (Ashoor et al, 2013). Therefore, it is important for women to understand that a positive result does not always mean that the baby is affected and a negative result does not always mean that the baby is not affected and appreciate the higher accuracy that invasive tests can provide.

e) NIPT has a 2% failed results

It has been reported that there is an approximately 2% of total pregnancies where NIPT is performed fails to deliver any results due to a number of reasons (Benn, Cuckle, & Pergament, 2013). In some studies in fact, this number has even been higher (Futch et al, 2013) drawing attention to several aspects that need to be taken into account when considering the pre-requisites in order for this screening test to be effective.

Firstly, a failed result may be associated with the test being carried out too early. In order for an abnormality to be reliably detected through this method, a 4-5% of foetal DNA in the maternal blood stream is required (RCOG, 2014; Wang et al, 2013). This is thought to correspond to the 10th week of gestation (although it is potentially detectable from the 5th week of gestation) and therefore the test should optimally be carried out from this point onwards since the amount of foetal DNA earlier in pregnancy may not be sufficient (Wang et al, 2013). However, between 10 and 21 gestational weeks the foetal DNA only marginally increases by about 0.1% on a weekly basis (overall 1% increase) while a greater and significant weekly increase (approximately 1%) can be expected after the 21st week, indicating that those with a failed original result would have to wait until the 21st week for a second blood draw to potentially produce a valid result. However, this entails a significant waiting and stressful period and it also does not allow substantial time for follow-up options (such as termination or preparation in the case of a positive result) to be considered carefully before a decision has to be made. Even though there may be some exceptional cases, current legislation allows a termination to be carried out up to 24 weeks (RCOG, 2010) and even if it is permitted later on the procedure becomes much more difficult and potentially more traumatic for the woman. Therefore, in order to increase the possibility of an accurate result it is imperative that the exact gestational age is established through a scan prior to any blood being drawn.

Another potential factor that has been linked with failed results is increased maternal weight which is shown to be negatively correlated with percentage of foetal DNA in the maternal serum (Wang et al, 2013). In other words, there is evidence to suggest that the higher a woman's weight the less likely it is to obtain reliable results as per the foetus' chromosomal status due to insufficient proportions of foetal DNA and this should be taken into consideration when offering women options for prenatal testing (Yagel, 2013). However, a threshold has not yet been determined for the exact maternal weight appropriate for a meaningful result and more studies need to explore this taking into account BMI levels so as to account for height in relation to weight as well.

To sum up, in order to increase the likelihood of a reliable NIPT result, time of blood draw (10th gestational week onwards) and maternal weight need to be carefully considered as they may have a powerful effect on the outcome of the test.

f) Range of abnormalities detectable via NIPT

NIPT currently only detects trisomies 13, 18, and 21 (and in some cases sex chromosome aneuploidy), whereas conventional karyotyping through amniocentesis and CVS provides detailed structural information on all 23 pairs of chromosomes. This means that many abnormalities currently being detected via invasive diagnostic tests cannot be detected via NIPT at least for the time being (Menezes et al, 2013). Therefore it is important for women to have a clear understanding of this and be appropriately supported and informed so that they can make a decision depending on the extent to which they wish to check their baby's health.

g) Ethical issues in relation to informed consent

In terms of informed consent, it is just as important as in the case of invasive tests even despite the exclusion of procedure related miscarriage. Therefore, this constitutes it a necessity for clear guidelines and prenatal/postnatal counselling to be provided to all women who have this test.

Also even though there is evidence suggesting that many women undergo the combined screening test because they consider it part of "routine" antenatal care (Fuchs & Peipert, 2005) rather than because of a rational decision they make after weighing up the pros and cons, when it comes to NIPT it is even more important to be clearly informed about the conditions being tested for and all associated information such as follow-up options (i.e. the option to terminate the pregnancy if Down Syndrome is diagnosed). The reason for this is mostly associated with the NIPT's level of sensitivity and the critical information it may disclose to the respective parents.

h) Costs

While considering the limitations of NIPT there is a substantial financial cost that needs to be considered. At the moment, NIPT costs between \$800 and \$2000 in the USA and from \$500 to \$1500 elsewhere in the world (Benn et al, 2013). While some private insurance companies may cover this cost, it is important to also take into consideration those covered by public health insurance who have been reported to be less likely to have NIPT because they are unable to fund it themselves (Vahanian et al, 2014). Therefore, while NIPT may become more cost-effective in the future and thus appeal to all populations the current financial demands place women who cannot afford it at a disadvantage.

1.3.2.3. Conclusion – key points regarding NIPT

Several large studies (Palomaki et al, 2012; Ashoor et al, 2013) have established NIPT as an effective new screening method but not one with the accuracy level of the current invasive diagnostic procedures, amniocentesis and CVS. Therefore, it is thus far recommended to use the term non-invasive prenatal testing (NIPT), rather than non-invasive prenatal diagnosis which

is misleading especially for those on the receiving end who are faced with an increasing number of options when it comes to antenatal care and testing.

NIPT is considered as a positive development in prenatal care, mainly due to the safety of the procedure, the increased accuracy and sensitivity of the test in comparison to the conventional combined test and the subsequent decrease in procedure-related loss of fetuses. This is due to the fact that this new screening method has the ability to more accurately detect the chromosomal status of the fetus and therefore only women who are at a very high risk will be faced with the option of further diagnostic tests (invasive) and their associated risks and difficult follow-up decisions.

However, this new development does not come without any concerns, mostly of an ethical nature. There are concerns that by making such a “safe” procedure so readily available, this may increase pressure upon women and constitute prenatal screening as a more routinised practice (Lewis, Silcock, & Chitty, 2013). As a result, this is likely to jeopardise informed consent as it is likely that women will feel less justified in wanting to turn down a blood test that entails no risks and thus potentially have the test in order to avoid social stigma and being frowned upon for not taking all available measures in order to identify any potential defects. The thin lines between being responsible and being a ‘good’ mother are well acknowledged in the literature and it has been previously suggested that blame is often attributed to mothers who fail to act in what is accepted as an appropriate manner (Ehrenreich & English, 1978; Oakley, 1984). Modern western society is very much “risk-orientated”, with the message given to women being that a no-risk pregnancy does not exist and therefore technological advances should be used in identifying potential risks to her unborn baby; these are defined by society and reflect what is considered to deviate from the “norm” (Beck, 1992). Considering that at the core of current Western belief systems lie science and technology it is perhaps not surprising that pregnancy and childbirth have become medicalised (Davis-Floyd, 1994). This has seen the focus centering on the female body as a “machine” that has to lead to a “successful” pregnancy and labour, diverting attention from the natural process of child-bearing and childbirth that is not only physical but rather involves two people, the mother and the baby. As a result of the expansion of medical technology, women have become more reliant on medical interventions as a source of information regarding the progress of their pregnancy and less trusting of their own maternal intuition and experience of the pregnancy (Jonsdottir, 2012). With the extensive use of technology, pregnancy is no longer viewed as a social process but rather becomes more technical with emotions of the mother often being neglected (Davis-Floyd, 2001).

In addition, there may be further social discrimination towards the disabled community and individuals with any chromosomal abnormality such as Down’s syndrome may suffer from the effects of this and feel yet more isolated within the society (Kaposy, 2013). The more medical technology is used to prevent babies with any congenital abnormality being born, the less “normal” these people will become within the society, potentially drawing negative responses and attitudes from others and stripping them of their human right to equality and diversion that

they certainly deserve. Such concerns have previously been voiced by health care staff who pointed out that the continuous changes in prenatal screening are likely to have an impact on the mother-foetal relationship placed within the wider societal context (Rapp, 1999). Likewise, Dumit and Davis-Floyd (2000) have pointed out that the increasing focus on the development of new technologies to assess the quality of the foetus are placing a strong emphasis on the production of “a perfect baby”, and with new tests becoming available this is likely to further be reinforced. Therefore, it is suggested that in order to prevent this from happening, the medicalisation of pregnancy should be re-visited and medical training should step back from solely focusing on the physical aspect of pregnancy and child-birth but rather adopt a more holistic view of the process that takes into consideration both the mother and the child as human beings with emotions rather than physical objects (Johanson, Newburn, & MacFarlane, 2002).

Nonetheless, so long as there is awareness of these risks preventative measures can be taken in order to ensure best practice with the least possible negative effects. A successful introduction of NIPT into antenatal care can be achieved, by the provision of clear guidelines and counselling strategies that will communicate all important information to women whilst also safeguarding informed consent on their behalf.

1.4. Invasive diagnostic testing options

The result of the first trimester screening test as well as that of NIPT, however, do not provide an accurate prenatal diagnosis but rather determine the likelihood of finding a chromosomal abnormality, (Schuchter et al, 2002). Following this process, and in order to confirm and diagnose the foetal abnormality suspected, further prenatal tests, such as amniocentesis and chorionic villus sampling (CVS), are required. Therefore, prenatal diagnosis is offered to all women who have positive antenatal screening results (Brajenovic – Milic et al, 2008).

These invasive tests (see Table 1.3), apart from providing a clear diagnosis, offer the couple several options:

- i. To explore the availability of further therapeutic intervention (i.e. surgery in the case of spina bifida);
- ii. To set up specific plans regarding the care of a child with special needs and to adjust their lifestyle accordingly;
- iii. To decide on the continuation or termination of the pregnancy.

Any decision requires full discussion with the physician and close relatives and may require additional genetic specialist advice.

Some individuals or couples may choose not to undergo preventive or other additional testing for various reasons, such as:

- i. Religious, moral or other personal reasons that do not allow them the choice of abortion, even in the case of a non-curable disorder being diagnosed;
- ii. Personal beliefs that the initial indication of the screening test is acceptable, taking into consideration future implications and consequences;
- iii. Fear of harming the foetus during the process.

Table 1.3

Invasive diagnostic options for antenatal testing

Trimester - Test	Timing (Weeks)	Detection Rate Of Down's Syndrome (%)	False- Positive Rate (%)	Sensitivity (%)	Specificity (%)
1 st - CVS	10-13	97.8	1 to 2	99.25	98.65
2 nd - Amniocentesis	15-18	99.4	0.1 to 0.6	99.4	99.5

1.4.1. Amniocentesis

One of the main applications of cytogenetics in clinical medicine is the prenatal diagnosis of chromosomal and other abnormalities of the foetus. Amniocentesis is the most common prenatal diagnostic method that is used for this purpose and is typically performed around the 16th week of gestation (15th- 18th). It was first applied in the 1950's and the first official diagnosis of Down's syndrome was announced in 1968. Since then its role has expanded to diagnose chromosomal abnormalities in general, as well as biochemical disorders, metabolic diseases and certain monogenic diseases (Daniilidis et al, 2008). What is more, the establishment of prenatal screening methods during the early stages of pregnancy (first trimester) has resulted in an increase in the number of amniocenteses that are being performed, as well as in the number of Chorionic Villus Sampling (CVS) tests, which constitute an alternative procedure.

Amniocentesis is an invasive procedure and involves the trans-abdominal insertion of a thin hollow needle into the uterus to withdraw from the amniotic sac a sample of amniotic fluid that includes foetal cells. The chromosome size and banding patterns of these foetal cells are then analysed in the lab and the arrangement of the 24 different chromosomes (22 pairs of autosomes and one pair of sex chromosomes) is used as a tool for the diagnosis of genetic disorders (Fajnzylber, Hotz, & Sanders, 2010). The reliability of amniocentesis ranges between 99.4 and 100% for the diagnosis of chromosomal abnormalities.

However, as with any invasive method, amniocentesis is also associated with specific complications such as amniotic fluid discharge, bleeding, amnionitida, foetal injury caused by the needle, and miscarriage. It is important to note that attempts are made to avoid injury to the foetus or placenta by means of ultrasound guidance, under which the surgery is performed.

Nevertheless, the risk of such complications, amongst others, will, to a certain extent, influence a patient's decision as to whether to accept or decline the procedure.

Before 1984, amniocentesis was only recommended to women over 35 years of age. This threshold was set because at this age the risk of having a child with DS is approximately equal to the risk of a procedure-related miscarriage, which is usually estimated to be 1%, and because the cost of offering amniocentesis was considered to be outweighed by the savings gained from avoiding the lifelong costs associated with the birth of an infant with DS (Moyer et al, 1999). However, this threshold implicitly assumes that women are equally worried about having a child with DS and a procedure-related miscarriage, something which has previously been proven not to be true (Harris, Nease, & Kuppermann, 2004), and also assumes that women would choose to abort a child with a serious congenital abnormality such as DS.

However, in recent years the discovery of serum and ultrasonographic markers provide ground for patient-specific assessment of risk level for foetal aneuploidy and allow for invasive testing to be more specifically targeted to high-risk women, thus leading to the avoidance of unnecessary invasive procedures (Geipel et al, 2003).

First trimester amniocentesis

First trimester amniocentesis is carried out between the 10th and 14th week of gestation. It is considered less secure than that of the second trimester and therefore is not as commonly used (Kennerknecht, Baur-Aubele, Grab, & Terende, 1992). It is technically more demanding and the insufficient retrieval of live embryonic cells required for the chromosomal analysis is more likely. In cases where an invasive diagnostic procedure is recommended for the 1st trimester, CVS is considered more appropriate.

1.4.2. Chorionic Villus Sampling (CVS)

Chorionic Villus Sampling (CVS) is an alternative to amniocentesis but is carried out earlier in the pregnancy, typically between 10 and 13 weeks of gestation (RCOG Greentop Guideline No 8, 2010). It is used for the prenatal diagnosis of chromosomal or genetic disorders in the foetus through sampling and testing of the placental tissue (*chorionic villus*) and always under the guidance of an ultrasound scan. More specifically, there are two approaches to CVS: *the trans-abdominal CVS*, where a needle is inserted through the abdomen, and *the trans-cervical CVS*, where a tube is inserted through the cervix. The position of the placenta usually determines which of these two methods will be used in order to better access the chorionic villi (Anderson & Brown, 2009). Although the benefit of CVS is that it provides early and definitive chromosomal analysis, in comparison to amniocentesis it has a slightly higher rate of miscarriage with an estimated percentage of 1-2% (RCOG, 2005).

However, according to current indications, the difference in the risk of miscarriage in relation to second trimester amniocentesis mostly concerns trans-cervical CVS (rather than trans-abdominal), which is much more technically demanding. Furthermore, regarding their diagnostic

value, there do not seem to be major differences between second trimester amniocentesis and CVS.

However, a practice that is still largely observed in some developing countries, such as India, is the use of such procedures for the purposes of sex selection and the abortion of female fetuses (Jha et al, 2006). In light of this evidence, most developed countries have established specific guidelines in order to ensure that the performance of such invasive procedures is in compliance with current medical indications (evidence-based approach). The long-term emotional and financial burdens that can be avoided with early diagnosis of a serious disease of the foetus and should the parents opt for termination of pregnancy, justify the costs associated with the performance of such prenatal diagnostic procedures.

1.5. Prenatally detectable genetic disorders

Most chromosomal abnormalities such as Down's syndrome and Edward's syndrome can be diagnosed by means of amniocentesis and CVS. It is also possible to diagnose diseases such as cystic fibrosis, congenital hemoglobinopathies such as thalassaemia and sickle cell disease, as well as Huntington and Tay-Sachs disease. Also, open lesions of the CNS such as spina bifida and anencephaly can be diagnosed through these methods.

However, it is worth stressing that no form of prenatal diagnosis can guarantee the birth of a perfectly healthy child, because only specific congenital disorders can be ruled out prenatally.

The method of PCR (polymerase chain reaction) is a technique that enables the creation of millions of copies of specific regions of the DNA molecule in a very short time and is a powerful tool for studying genetic material, including disease-causing genes. It has been incorporated in the process of amniocentesis (amnio-PCR) and provides definitive diagnosis of the most common chromosomal abnormalities within 24-48 hours (Baig et al, 2010).

Some of the foetal disorders that can be detected through amniocentesis and/or CVS are listed below.

1.5.1. Chromosomal disorders

1.5.1.1. Trisomy 21 (Down's syndrome)

Trisomy 21 is most frequent chromosome aberration at birth and is associated with various physical abnormalities and diseases (Siegrist, Cousin, & Keller, 2008). More specifically, infants with DS suffer from general hypotonia (poor muscle strength and elasticity), are more likely to suffer from congenital malformations (heart problems being the most common), and are also at an increased risk of mental and growth retardation (Fajnzylber et al, 2010). Even though some therapies are available for specific malformations, there is no effective treatment for the cognitive problems associated with this condition, making these children dependent on their parents / carers for life. What is more, life expectancy for DS children in developing countries is

limited to approximately 35 years, although medical advances have increased this to approximately 55 years in the USA and other Western countries (Dick, 1996). Nevertheless, taking into consideration the lifelong treatments and psychological implications, which include maternal depression and difficulties with marital and sibling relationships, DS is a costly disease for a family, both on a financial and on a psychological level. Therefore, many parents are interested in the prenatal detection of affected fetuses in order either to adapt to the circumstances of having a child with a disability, to establish plans for special prenatal and post-natal care, or to terminate the pregnancy, which is considered legal up to 24 weeks if a foetal abnormality is detected (France, Wyke, Ziebland, Entwistle, & Hunt, 2011).

1.5.1.2. Trisomy 18 (Edward's syndrome)

Trisomy 18 is caused by the presence of an extra 18th chromosome in the infant's cells and carries with it a very low life expectancy, resulting from various internal organ disorders such as heart abnormalities or kidney malformations (Palomaki, 2011). It is invariably characterised by increased foetal nuchal translucency (NT), in association with decreased maternal serum free β -human Chorionic Gonadotropin (β -hCG) and pregnancy-associated plasma protein A (PAPP-A) (Sherod, Sebire, Soares, Snijders, & Nicolaides, 1997).

1.5.1.3. Trisomy 13 (Patau syndrome)

Trisomy 13 is characterised by the presence of an extra 13th chromosome, which disrupts the normal course of development by causing heart or kidney malformations and severe intellectual disability (Pitukkiyironnakorn, Promsonthi, Panburana, Rangsiprakarn & Chittacharoen, 2008). Like the previous disorder, it is characterised by decreased β -hCG, PAPP-A, and increased NT (Spencer, Charas, Skentou, Liao, & Nicolaides, 2000).

Other examples of chromosomal abnormalities which are prenatally detectable include: a shift of genetic material from chromosome to chromosome without loss or excess material, mosaicism (where cells within one individual have a different genetic makeup), chimerism (a rare condition whereby a person has more than one set of DNA), and abnormal sex chromosomes X and Y. The latter involves cases such as Turner syndrome, which is characterised by a lack of sex chromosomes (45 instead of 46, 44 XO) and whose main features include vrachysomia and infertility. Other sex chromosome abnormalities include the triple Y or X chromosome (superman, superwoman) and the syndrome 'Fragile X chromosome'.

1.5.2. Autosomal disorders

Autosomal disorders fall under the umbrella of single gene disorders (also called 'monogenic disorders'), which are inherited genetic diseases caused by a single gene defect (Weatherall, 2000). They are further divided into the *dominant* type (where the abnormal gene from only one parent is required in order for a child to inherit the disease) and the *recessive* type (where a copy of an abnormal gene from each parent is required for the disease to be inherited). Examples of autosomal dominant disorders include Huntington's disease and Marfan's

syndrome, whereas some recessive examples include congenital hemoglobinopathies (sickle cell disease and thalassaemia).

1.5.2.1. Sickle cell disease (SCD)

Sickle cell disease is an autosomal recessive genetic blood disorder which is caused by an abnormal type of haemoglobin. This haemoglobin – namely haemoglobin S – causes the red blood cells to acquire an abnormal, rigid, sickle shape and, as a result, to deliver less oxygen to the body's tissues. What is more, these sickle-shaped cells are more prone to adhere to small blood vessels and interrupt normal blood flow (Rees, Williams & Gladwin, 2010).

The vast majority of people with sickle cell disease will have painful episodes, which are called crises and have varying degrees of severity and duration (lasting from hours to whole days). Other conditions associated with SCD include chronic anaemia, jaundice, organ failure, infections, and strokes (RCOG, 2005). There is no cure for SCD, but rather patients need ongoing treatment in order to manage their symptoms and limit the amount of crises they experience. All in all, SCD may lead to various acute or chronic complications, many of which have a high mortality rate. Nonetheless, the life expectancy for people with this condition in the UK has increased from an estimated 42 years to 53-60 years, due to medical advances and better management of the disease (Gill, Lavin & Sim, 2010).

With regard to diagnosis of SCD, in most parts of the world prenatal screening is offered to women in order to establish the parental haemoglobin gene mutation. If positive results are obtained, an amniocentesis or CVS is offered as an option in order to obtain a definitive diagnosis, which in turn, may help prevent complications and provide information for family planning (Steinberg, 2011).

1.5.2.1. Thalassaemia

Thalassaemia is another type of inherited autosomal recessive blood disorder, which is mainly characterised by anaemia, hence a decrease in the amount of red blood cells or in the amount of haemoglobin in the blood (Panomai et al, 2010).

Unlike the qualitative nature of the implications of SCD, where an incorrect functioning of the β globin takes place, the problems associated with thalassaemia are of a quantitative nature, with an underproduction of one of the two globin chains (α or β) which make up the haemoglobin. Thus, there are two major forms of this disease which take their names according to which of the two chains of the haemoglobin molecule is affected: *alpha-thalassaemia* and *beta-thalassaemia* respectively (Tan et al, 2010).

In the UK, as in many other parts of the world, a blood test is offered to all pregnant women as part of their antenatal care in order to screen for the presence of a thalassaemia gene. If the result is positive, a test is subsequently offered to the father of the unborn child, and if the combination of the parental results indicates a risk for the foetus, further invasive diagnostic

tests (amniocentesis or CVS) are offered as a means of providing an accurate diagnosis for the baby (RCOG, 2005). Follow-up options, such as continuation or termination of an affected pregnancy, are discussed with the couple.

1.5.3. Metabolic diseases

Inherited Metabolic Diseases (IMDs), which are also autosomal recessive inherited disorders, include those affecting the metabolism of amino acids, organic acids, fatty acids, carbohydrate, and the urea cycle. Some of these may cause serious complications during pregnancy, affecting either the mother and/or the foetus (Preece & Green, 2002).

For IMDs where the risk for serious complications is established, optimal treatment may lead to a better maternal and foetal outcome. One such case is that of phenylketonuria (PKU), whereby patients are unable to convert phenylalanine to tyrosine in the liver due to a recessively inherited defect in the enzyme phenylalanine hydroxylase. Symptoms of untreated PKU include serious developmental delay, disturbed behaviour and hyperactivity in older children. However, like most IMDs, phenylketonuria can be diagnosed prenatally through amniocentesis or CVS, and as for other conditions, a termination of pregnancy is an option in the case of an affected foetus. Nevertheless, even for those who do not wish to terminate a pregnancy, regardless of the result, a prenatal confirmation of an affected foetus may prove beneficial for the better management of the condition by setting up plans for specific treatments during pregnancy and/or at birth (Preece & Green, 2002).

1.5.3.1. Disorders of the musculoskeletal system

Muscular Dystrophies (MD) are a progressively degenerative group of inherited neuromuscular disorders that involve muscle weakness and the loss of muscle tissue (Sewry, 2010). Some types of MD cause little disability, while others are more severe and lead to a premature death. One such example is Duchenne Muscular Dystrophy (DMD), which affects boys and is characterised by progressive muscle degeneration. This leads to loss of independent ambulation by the age of 13 years and several other medical complications such as progressive arm and hand dysfunction, speech problems, respiratory insufficiency, and ultimately death in the late teens (Spies, Shipper, Nollet & Abma, 2010). DMD is a result of a defect in the dystrophin gene which is caused by mutations on the X chromosome. Invasive tests such as amniocentesis or CVS can be used for prenatal diagnosis of this disease, followed by the option of terminating an affected pregnancy (Bushby et al, 2010).

1.5.4. Intellectual disabilities

1.5.4.1. Fragile X syndrome

Fragile X is the most common inherited cause of intellectual disability involving changes in part of the X chromosome, and more specifically a gene called FMR1. Although both sexes can be affected, since males only have one X chromosome a single fragile X is likely to affect them more severely than females (Sherman, Pletcher & Driscoll, 2005).

As a result of Fragile X syndrome, several cognitive and intellectual limitations manifest, including language delays, problems with working and short-memory, executive function, and mathematic and visuospatial abilities. From a behavioural aspect, autistic-like features (i.e. hand flapping and eye-contact avoidance) are also commonly observed, alongside impaired social skills and emotional problems such as anxiety and mood disorders, hyperactivity and aggressive behaviour (Garber, Visootsak & Warren, 2008).

Since the specific gene responsible for this syndrome was identified in 1991, it has become routine clinical practice to offer screening to affected families (where the mother is a known carrier) and follow these up with the offer of invasive diagnostic procedures (amniocentesis or CVS) for those who are considered at high risk (Pesso et al, 2000).

1.5.5. Neural tube defects

Neural tube defects such as *spina bifida*, which is an incompletely enclosed spinal cord, and *anencephaly*, which involves the absence of a large part of the brain or skull, are two less common but more fatal genetic disorders. It is important to note that these can be detected through prenatal screening and testing, but only via amniocentesis and not CVS (Fajnzylber et al, 2010).

To sum up, current guidelines from the UK RCOG and ACOG recommend that all pregnant women, regardless of their age, should be offered prenatal screening for congenital abnormalities. Those who receive positive results, and hence are considered to be at high risk of foetal aneuploidy, should then be given the option of undergoing an invasive prenatal diagnostic test – most often in the form of amniocentesis – in order to confirm or disconfirm the suspected pathology. However, at this point it is important to highlight the importance that is placed on shared decision-making when it comes to medical decisions.

1.6. Shared decision-making

Shared decision-making is a process in which a health-care decision is jointly made by a clinician and a patient, and is based on evidence-based information about choices, outcomes and uncertainties combined with the patient's informed preferences (Coulter & Collins, 2011). While shared decision-making is mostly thought of in relation to major treatment procedures, it

is in fact relevant in almost every clinical encounter including screening and diagnostic tests such as CVS and amniocentesis. Relevant professional regulatory bodies, such as the Health Professions Council (HPC) and the General Medical Council (GMC), characterise shared decision-making as an ethical imperative in all medical decisions. According to the *Good Medical Practice* guidance for all doctors:

“Whatever the context in which medical decisions are made, you must work in partnership with your patients to ensure good care. In so doing, you must listen to patients and respect their views about their health, discuss with patients what their diagnosis, prognosis, treatment and care involve; share with patients the information they want or need in order to make decisions; maximise patients’ opportunities, and their ability, to make decisions for themselves; respect patients’ decisions.” (General Medical Council, 2009).

What is more, an important element of any medical decision is that it has to be an “informed choice” of the patient, which, according to O'Connor and O'Brien Pallas (1989), *“is one that is based on relevant knowledge, is consistent with the decision-maker’s values and is behaviourally implemented”* (pp.486-496).

Understanding how to facilitate informed choices in healthcare settings is of great interest to those taking a psychological perspective on health behaviour, and the importance of this in clinical practice is evidenced in an improved patient-physician relationship and satisfaction, as well as better patient outcomes (Legare et al, 2011). In addition, considering that most medical decisions occur in an uncertain context, a shared decision-making process is considered to improve the quality of the patient’s decision by increasing knowledge and clarifying patient preferences (O'Connor et al, 2009).

1.7. Decision making process in prenatal testing

1.7.1. The role of Health Psychology

In prenatal diagnosis, the need for a decision-making process that is consistent with personal values is imperative as it concerns a complex and multi-faceted issue that may have lifelong consequences for numerous people. This includes the woman having to make the decision to undergo a prenatal test or not, the unborn fetus, and those of the wider family involved such as the partner, and other children previously born into the family. Similarly, to the aforementioned professional regulatory bodies, and in line with the British Medical Association’s guidelines on informed consent, the National Screening Committee states that all patients have a right to be fully informed of any testing offered to them, including any risks or alternatives, before they decide whether to agree to the proposed test or not (Marteau, Dormandy & Michie, 2001). This means that women who are offered the option of amniocentesis, CVS or NIPT should be fully informed of the purpose of the tests, the accuracy of the findings, the risks and uncertainties attached to the process – such as the risk of miscarriage with invasive tests - and any follow-up

plans which involve a choice of terminating or continuing with the pregnancy (GMC, 1999). However, despite these rules and regulations that -theoretically at least- guide clinical practice, there is evidence to suggest that pregnant women do not always possess the required knowledge and understanding of the tests being offered to them, putting into question the extent to which they are actually in a position to make an informed choice (Green, Hewison, Bekker, Bryant, & Cuckle, 2004).

Nevertheless, regardless of the complexity of the process and its stakes, NIPT as well as invasive diagnostic tests may offer benefits to women who participate, and therefore it is important to look into the specific factors that are implicated in the decision-making process, which may contribute to test use, benefiting both individuals and medical science in general (Tercyak, Johnson, Roberts, & Cruz, 2001).

Health psychology can undoubtedly play an important role in this field. First of all, the theoretical models, such as Social Learning Theory (Bandura, 1977), combined with the extensive research capacity within this discipline, may offer the foundations for identifying the variables that influence women's decisions. For example, in the past the Theory of Planned Behaviour (TPB; Ajzen, 1991) has been successfully used to explain and predict a range of behaviours including the uptake of prenatal screening (Sapp et al, 2010). Furthermore, health psychologists may also contribute on a more practical level by developing interventions aimed either directly at women or at doctors in order to maximise informed decision-making when it comes to deciding whether or not to undergo an invasive prenatal diagnostic procedure.

1.7.2. An overview of factors involved in the decision-making process

A review of the literature suggests that the uptake of prenatal tests, such as amniocentesis, CVS, and NIPT is related to both *rational variables*, such as knowledge about the specific procedure, and *emotional variables*, such as anxiety levels, social norms, and other internalised values which are reflected in an individual's *attitudes*. The latter can be defined as a person's favourableness or unfavourableness towards a specific concept (Lesser & Rabinowitz, 2001).

To be more specific, previous studies have stated that *knowledge* is a prerequisite for any woman making an informed decision about taking up any of the prenatal tests that are being offered to her. This encompasses knowledge of: the purpose of a given test, the likelihood of a positive or negative outcome, the risks attached to the diagnostic procedure, and follow-up plans including the offer of abortion in the case of an affected foetus (Marteau, Johnston & Plenicar, 1988). Within the context of prenatal tests, and since uptake is voluntary, the purpose of the information provided to women faced with this decision is to facilitate informed decisions (Shoonen et al, 2011). However, regarding its predictive validity, there have been conflicting findings in the literature. Hence, some studies have found that women who had an elective amniocentesis were more knowledgeable about the diagnostic test than those who chose not to have the procedure (Lesser & Rabinowitz, 2001), while others have found that knowledge was not predictive of women's decision outcome (Michie, Dormandy, & Marteau, 2002). As far as

NIPT is concerned, whilst most women have been found to have good knowledge of the main properties of this test, several misunderstandings have also been reported, such as that NIPT is 100%, that it can detect conditions such as spina bifida and that the turnaround time for the results is shorter than that for invasive diagnostic tests (Lewis et al, 2016). Lower levels of knowledge regarding NIPT have been associated to women declining the test (Farrell, Hawkins, Barragan, Hudgins, & Taylor, 2015).

The second set of variables that has been implicated in the decision-making process regarding uptake of invasive and non-invasive tests includes intrinsic values as reflected in women's *attitudes* towards specific concepts. Attitudes can be divided into two broad categories: attitudes towards specific *targets*, which in the current context might involve attitudes towards having a baby with Down's syndrome, and attitudes towards *behaviours that are directed towards specific targets*, which in this instance may consist of attitudes towards having NIPT or a diagnostic test for Down's syndrome (Bryant, Green & Hewison, 2010). Prior studies have suggested an overwhelmingly positive attitude of women towards prenatal testing in general and a tendency of women to report a positive attitude even towards having the recently developed NIPT (Sahlin et al, 2016). Nonetheless, further research is required to establish these findings, considering that NIPT has only been recently introduced into clinical practice.

In health psychology, rational expectancy-value models such as the Theory of Reasoned Action (TRA; Ajzen & Fishbein, 1980) and The Theory of Planned Behaviour (Ajzen, 1991), which have been mostly used in order to explore the relationship between attitudes and behaviour, focus on predicting behaviour via attitudes toward the specific behaviour (i.e. undergoing a prenatal test) rather than attitudes towards the behavioural target (i.e. having a child with DS). However, a study by Bryant et al (2010) demonstrated that understanding an individual's attitudes towards a tested-for condition, such as Down's syndrome, alongside the burden attached to having a baby with such a condition, may help predict their intentions of using prenatal diagnostic tests. Therefore, when considering influences on amniocentesis/CVS or NIPT uptake it is important to explore not only attitudes towards having the actual test, but also attitudes towards having a baby with DS.

A further attitude that has been associated with the rejection of amniocentesis/CVS is the *attitude towards miscarriage* as a result of the diagnostic procedure, with women who are more concerned over the possible risk of miscarriage being more likely to decline the diagnostic test (Santalahti, P., Hemminki, E., Latikka, A.M., & Ryyanen, 1997). Conversely, the absence of risk when it comes to NIPT has been found to influence women's positive attitude towards this testing method (Lewis et al, 2016) and has been associated with uptake of this testing approach (Barrett, Advani, Chitty, & Choolani, 2016).

Quite relevant to this is the suggestion by Marteau (1990) that patients' attitudes towards doctors and medicine (which she categorised as positive versus negative) may prove useful in predicting health-related behaviours, such as attending for screening. However, later studies

reported that refusal of prenatal screening did not necessarily signify rejection of medical science and technology; it was observed that while women who declined amniocentesis/ CVS tended to distrust biomedicine and place more trust in experiential sources of information – such as feeling “normal” movements of the baby in the womb – and vice versa for those accepting the diagnostic test, neither of the two groups placed authoritative power solely in one source or the other. Rather, they both drew on the biomedical model to account for their decision, simply focusing on different elements of it whilst also taking into account experiential information, to either a greater or lesser extent (Lippman, 1999; Markens, Browner & Press, 1999). That said, a recent study found that trust in doctors and medicine was fundamental in shaping women’s decisions to accept or decline amniocentesis, drawing attention back to the suggestion initially raised by Marteau (Markens, Browner & Preloran, 2010).

Another independent factor that has been positively associated with amniocentesis/ CVS and NIPT uptake is *women’s perception of being at an increased risk* of having a baby with Down syndrome, regardless of their actual risk level (Lewis et al, 2016; Marteau et al, 1991). However, this finding has not been consistent across studies, with Tercyak et al (2001) reporting that neither actual nor perceived risk was related to test uptake.

Moreover, although less documented in the literature, it has been proposed that the notion of “*anticipated decision regret*” might play an important role in the choice of having a prenatal test (Tymstra, 2007). The reasoning behind this construct is that people will choose to have a test done in order to avoid being confronted later on with negative feelings that may result from what proves to have been a wrong choice; for instance, expectant mothers might feel responsible for giving birth to a child with a congenital abnormality if this could have been prevented by her accepting an invasive test when it was offered to her.

Another factor that is possibly implicated in the amniocentesis/ CVS decision-making process is *health locus of control* (HLOC), which, according to Rotter’s Social Learning Theory (1966), is classified as *internal*, when an individual’s appraisal of an outcome is perceived as a direct result of their own behaviour, or *external*, when a person believes that the outcome of a situation is under the control of powerful others (i.e. doctors), or is determined by random forces, such as chance (Sanders, 1989). HLOC is a construct that has received much research attention by health psychologists, who have highlighted its importance by associating beliefs about internal versus external control with various health-related behaviours (Strickland, 1978). With regard to amniocentesis, an *internal* or *medical profession/external locus of control* has been associated with acceptance of the test, whereas a *chance/external locus of control* has been associated with refusal of the procedure (Lumley, Zamerowski, Jackson, Dukes & Sullivan, 2006; Punales, 2005); this suggests that women who believe themselves or their doctors to be in control are more likely to undergo invasive testing, as opposed to women who attribute outcomes to chance.

Relevant to this is the concept of “*subjective norms*”, which has also been reported in previous studies, whereby a woman will choose to have a prenatal test regardless of her own attitude towards it simply because she feels pressured into it by her social environment (Michie et al, 2002). The most influential sources reported in the literature are partners, doctors in antenatal care and to a slightly lesser extent family and friends (Georgsson et al, 2016). Yet, the evidence is not clear, with some studies reporting that the majority of women are not affected by others and that the decision to undergo NIPT or not is their own (Sahlin et al, 2016). The term “technological imperative” which is widely spread throughout Westernised parts of the world also mirrors this tendency of people to worship technology and to conform to societal pressure of considering normative the acceptance of any technological intervention that becomes available (Gillick, 2007). And even though the choice to undergo a prenatal test such as amniocentesis/CVS or NIPT is up to the woman herself, it appears that nowadays the maternal and medical norms are such that any such recommendations are perceived as orders to be followed. Nevertheless, the possible implications of technological interventions need to be addressed and alternatives, such as non-use, be considered if a truly informed decision is to be made (McCoyd, 2010).

Finally, *anxiety* is a factor that has been implicated in numerous studies regarding prenatal screening and diagnostic tests. However, the results have been conflicting with some studies reporting it as a factor contributing to the uptake of amniocentesis in order for the woman to gain reassurance about her baby’s health (Lesser & Rabinowitz, 2001), while others associate elevated anxiety levels with rejection of amniocentesis, as a result of concern over the possibility of foetal injury, anticipated pain during the procedure, or the outcome of the test (Ilgin-Ruhi et al., 2005; Karasahin, Gezgin & Alanbay, 2008). As far as NIPT is concerned, anxiety over foetal health and women’s own coping abilities has been associated with uptake of this testing method (Lewis et al, 2016). Understanding how anxiety interacts with other psychosocial factors is relevant to the objective of this study.

1.8. Aim of the study

Although all the aforementioned variables have been identified through various studies that have been carried out regarding the uptake of prenatal screening and amniocentesis, the vast majority of these studies lack a theoretical framework, focusing instead on isolated variables. Also, it has been suggested that due to similarities in key constructs between the leading models of health behaviour, an integrative approach using a combination of several models may better explain specific health behaviours (Shiloh, 2006). Therefore, the aim of this study will be to take a more holistic approach and use a combination of psychological models in developing a questionnaire aimed at identifying those variables that are most significant in a woman’s decision to have NIPT, an invasive test or no further testing following the routine first trimester combined screening test.

1.9. Study hypotheses

- Women who perceive themselves to be at an increased risk of having a baby with a chromosomal abnormality will be more likely to have an invasive test or NIPT.
- Women who feel pressured by their social environment into having an invasive test or NIPT will be more likely to opt in for one of these tests.
- Women who have an increased awareness of NIPT and invasive diagnostic tests will be more likely to have one of these tests.
- Women with a positive attitude towards undergoing an invasive test or NIPT will be more likely to have one of these tests.
- Women who attach a greater burden to having a child with a chromosomal abnormality will be more likely to have an invasive diagnostic test and/or NIPT.
- Women with a positive attitude towards doctors and medicine will be more likely to choose to have an invasive diagnostic test or NIPT.
- Women with an internal or medical professional/external locus of control will be more likely to have an invasive test or NIPT.
- Women who are concerned over losing their baby as a result of a diagnostic procedure will be less likely to undergo an invasive diagnostic test and more likely to have NIPT.

2. Chapter Two: Methods – Pilot Study and Validation of Questionnaire

2.1. Development of questionnaire

2.1.1. Theoretical framework

Following the literature findings described in Chapter 1, a questionnaire was developed for the purposes of this study. Adopting a holistic approach, this was informed by a combination of the following theoretical models:

- a) The “*subjective expected utility model*” (SEU; Savage, 1954) which is the leading decision-making model in the presence of risk, according to which an optimal decision maximises expected utility (Shiloh, 2006);
- b) *Ley’s Cognitive Hypothesis* (1989), according to which, in order to improve compliance, a certain level of awareness regarding the specific situation is required;
- c) The *Health Belief Model* (Rosenstock, 1966), which is used to describe behaviour or decision-making under the circumstances of uncertainty, and according to which, health behaviour is determined by beliefs regarding: *perceived susceptibility*, *perceived severity*, *costs*, and *benefits*; in other words, a person is considered more likely to carry out a health behaviour if they perceive the threat of the disease to be relevant to them and if the benefits of this behaviour are perceived to outweigh the costs (Armitage & Conner, 2000);
- d) The *Theory of Planned Behaviour* (Ajzen, 1988), which predicts a person’s intention to perform a specific behaviour based on their *attitudes* towards this behaviour, their *perceived behavioural control* over the final outcome, and the influence of *subjective norms*, which is a term used to describe a person’s beliefs about what salient others think he/she should do;

And finally,

Other factors that were also addressed in the questionnaire and have been earlier described (see Chapter 1) include: the construct of *anticipated decision regret*, *Health Locus of Control*, *anxiety*, and women’s socio-demographic and medical backgrounds.

2.1.2. Study variables measured

Based on the theoretical framework described in the section above, all variables to be included in the study were identified (see Table 2.1).

Table 2.1

Variables to be studied and their respective theoretical frameworks

Variable	Corresponding theory
1. Knowledge (regarding amniocentesis)	Ley's Cognitive Hypothesis
2. Attitude towards having amniocentesis	Theory of Planned Behaviour
3. Attitude towards amniocentesis	Health Belief Model
4. Attitude toward having a baby with a serious abnormality (attached burden)	Health Belief Model
5. Attitude towards miscarriage as a result of amniocentesis	Health Belief Model
6. Perceived risk of having a baby with a serious abnormality	Health Belief Model
7. Perceived behavioural control	Theory of Planned Behaviour
8. Anticipated decision regret	-
9. Subjective norms	Theory of Planned Behaviour
10. Attitudes towards doctors and medicine	Theory of Planned Behaviour
11. Anxiety	-
12. Health Locus of Control (HLOC)	-

Each of the identified variables presented in Table 2.1 were then explored in relation to existing measures and their psychometric properties and a comprehensive questionnaire was developed including the following sections:

a) Section A: Knowledge

This section consisted of four items that examined women's knowledge in relation to the purpose and reliability of amniocentesis, the risk for miscarriage associated with invasive tests, and follow-up options. Two of the items were multiple choices and two were 'true' or 'false'. The score scale ranges from zero (no correct answers) to 4 (all correct answers) with higher scores indicating greater awareness in relation to invasive tests. Similar scales to this have previously been used to assess knowledge of prenatal screening tests in general rather than focusing on invasive tests (Brajenovic-Millic et al, 2008; Marteau et al, 1988).

b) Section B: You and amniocentesis / CVS

This section involved the measurement of the following internalised variables:

- i. *Attitudes towards having amniocentesis/ CVS* was measured by a scale that consisted of four 5-point semantic differentials as follows: "For me, having amniocentesis/ CVS

would be... not at all beneficial-very beneficial / extremely unpleasant-not at all unpleasant / not at all reassuring-very reassuring / not at all frightening-very frightening". Participants' responses were measured on a five point Likert scale ranging from 1(very negative attitude) to 5 (very positive attitude).

- ii. *Attitudes towards amniocentesis/CVS* was measured by two items using a 5-point Likert scale ranging from 1(=strongly disagree) to 5(=strongly agree). Higher scores indicate a more negative attitude towards amniocentesis/CVS.
- iii. *Attitude towards miscarriage as a result of amniocentesis/CVS* was measured using a 5-point Likert scale ranging from 1(=extremely bad) to 5(=not at all bad). Higher scores indicate a more negative attitude towards miscarriage.
- iv. *Perceived severity* was measured using a 5-point Likert scale ranging from 1(=strongly disagree) to 5(=strongly agree). Higher scores indicate a higher perceived severity of chromosomal disorders such as Down's syndrome.
- v. *Anticipated decision regret* was measured using a 5-point Likert scale ranging from 1(=strongly disagree) to 5(=strongly agree). Higher scores indicate higher intentions to use any tests available.
- vi. *Burden attached to having a child with a serious abnormality* was measured using a 5-point Likert scale ranging from 1(="very good") to 5(="very bad"), with higher scores indicating greater burden attached.
- vii. *Perceived risk of having a child with a serious abnormality* was measured using a 5-point Likert scale ranging from 1("not at all likely") to 5("very likely"). Higher scores indicate greater perceived risk.
- viii. *Perceived behavioural control* was measured using a short version of a scale used in a previous study (Berkenstadt et al, 1999). This consisted of three items rated on a 5-point Likert scale and ranging from 1(=strongly disagree) to 5(=strongly agree). Higher scores indicate greater perceived behavioural control.

For all the items above a sixth option ("Don't know") was also provided.

c) Section C: Others and amniocentesis / CVS

This section included a scale adapted from a previous study on prenatal screening (van der Berg, 2008) and measured *subjective norms* by assessing normative beliefs and weighing them for motivation to comply (Ajzen, 1991). Normative beliefs were assessed for the woman's partner and her midwife/obstetrician by two 5-point items. For example: "*If it is offered to me, I think my partner will want me to...*" with answer options ranging from "*certainly decline amniocentesis/CVS*" to "*certainly accept amniocentesis/CVS*". The respondent's motivation to comply with each of these normative beliefs was measured by a 5-point item as follows: "*I find my partner's opinion about accepting or declining the test...*" and answer options ranging from "*very important*" to "*not at all important*". An overall

subjective norm scale of the two referents together is estimated by calculating the mean of the two products of normative beliefs with motivation to comply and the scale ranging from 1 (=strong subjective norm to decline amniocentesis/CVS) to 5 (=strong subjective norm to accept amniocentesis/CVS)

d) *Section D: How you are feeling*

This section measured anxiety using the anxiety scale from the Hospital and Anxiety Scale (HADS; Zigmond & Snaith, 1983). This includes 7 items rated on a 4-point likert scale with scores for each item ranging from 0 to 3. A mean score is then calculated across all items, meaning that a respondent can score between 0 and 21, with higher scores indicating greater levels of anxiety. A cut off score of 8 has been established across numerous studies indicating that individuals scoring above this score are clinically anxious (Bjelland, Dahl, Haug, & Neckelmann, 2002).

e) *Section E: Attitudes towards doctors and medicine*

This is a scale developed by Marteau (1990) and aims to specifically measure attitudes towards effectiveness of medicine in promoting health and attitudes towards the effectiveness of doctors in promoting health. It consists of 19 items rated on a scale from 1(=strongly disagree) to 5(=strongly agree).

f) *Section F: Beliefs about illness:*

This section consists of the Health Locus of Control Scale (Walston & Walston, 1981) which is formed by the following three 6-item subscales: internality; powerful others externality; and chance externality. Each of these scales is rated on a 5-point likert scale ranging from 1(=strongly disagree) to 5(=strongly agree) and they are scored independently from one another.

g) *Section G: You and your family*

This section covered demographic information (i.e. age, ethnicity, religion), socio-economic status (i.e. marital status, level of education, occupation, household annual income) and medical history information (i.e. prior miscarriages or termination of pregnancy, prior history of amniocentesis, etc.). This information is important in order to be able to control for external factors and be able to focus on the specific psycho-social variables under study. However, the demographics section was strategically placed at the end of the questionnaire so as to ensure that participants gave priority to the actual questionnaire should they return it incomplete.

h) Screening measure

At the end of the demographics section a brief screening measure for mental health issues was included. This includes a mixture of ten health-related issues covering both, mental health, such as depression and schizophrenia, and common health problems, such as migraine and allergies. The aim of the common health problems was to slightly mask the emphasis on asking questions just about mental health. Participants were also asked to state any medication they were taking at the time. The purpose of this screening tool was to allow for exclusion of those who were suffering from any sort of mental health issue, which may have impacted on their responses to the other scales of the questionnaire.

See Appendix 1 for a copy of the original questionnaire.

2.1.3. Procedure

Following ethical approval from the NHS REC committee and the King's College Hospital R&D, women were invited to participate in the study through the post. The questionnaire and the accompanying documents (consent form - see Appendix 2, information sheet – see Appendix 3, debrief form – see Appendix 4) were sent together with the appointment letters that were posted for their first trimester scan. Participants were given the option to either post back the completed questionnaire and consent form (using a pre-stamped envelope enclosed) or bring them in themselves to hand over to a member of staff when they attended their scan appointment.

In an attempt to increase the response rate, after an initial trial, incentives were added to the study after ethical approval was sought from the aforementioned ethical committees. The incentives comprised of:

- a) A voucher (see Appendix 5) for respondents to complete their preferred method of contact and return with their questionnaire so as to be entered into a prize draw for a £200 voucher to spend at a big maternity chain-store. and,
- b) A sample of Pregnacare folic acid & vitamin supplements that was included as a token of gratitude with every questionnaire sent out to candidates through the post.

Upon return of the completed questionnaires, these were securely stored –unopened- at KCH and the chief investigator collected them for analysis and safe storage. Following the analysis of the data, the questionnaires (which were anonymous) were stored in locked cabinets and kept separately from the consent forms to which they could only be linked via a participant ID number allocated by the chief investigator. This ensured that all responses were unidentifiable and only the chief investigator could have access to the questionnaires and personal information if required.

2.1.4. Participants

Participants were all patients of King's College Hospital (KCH), who were in the first trimester of their pregnancy and had not yet attended for their first scan. In line with the inclusion criteria they were all above 18 years of age, they could speak and write English, and were not suffering from any kind of mental health issues. A total of 58 valid questionnaires were collected and included in the analysis.

2.2. Principal Component Analysis (PCA) on pilot study questionnaire

2.2.1. Background and main goals

As mentioned above, the questionnaire administered during the pilot study consisted of some already established and validated scales (the Health Locus of Control Scale; the HADS – anxiety scale; and, the attitudes towards doctors and medicine questionnaire) whilst other questions were also included in an attempt to explore additional variables that may potentially influence women's decision making process regarding uptake of amniocentesis/CVS. The latter however, were not part of a previously standardised questionnaire so it was considered plausible to subject them to further statistical assessment through conducting a factor analysis.

The main goal for this was to reduce the number of items into clusters of variables or otherwise named 'factors' that will be stronger statistically and more meaningful. This process would hopefully lead to a shorter and more efficient questionnaire but not at the cost of any important information, whilst also facilitating analysis and interpretation of the findings. The newly revised version is planned to be used for the main study in order to retrieve all the necessary data from participants without being overly exhausting and time-consuming.

In terms of factor analysis there are many different types involving a multitude of different techniques, but for the purposes of this study a PCA was carried out. PCA has its roots back to Pearson (1901) making it the oldest but also the most popular multivariate statistical technique which is used in almost all scientific disciplines (Abdi & Williams, 2010). Its wide use has led to it being characterised as a well-established technique for dimensionality reduction (Tipping & Bishop, 1999) thus justifying its use in this pilot study.

As summarised by Abdi & Williams (2010) the goals of PCA are:

- a) To extract the most important information from the data table;*
- b) To compress the size of the data set by keeping only this important information;*
- c) To simplify the description of the data set; and*
- d) To analyse the structure of the observations and the variables.*

The PCA was carried out using the statistical software SPSS and the results are considered below in order to validate the suitability of this method for our specific data-set and extract suitable factors for interpretation. It is important to note here that the process of PCA in SPSS was repeated until all weak variables were removed and only those suitable for interpretation were retained.

2.2.2. Key findings

Key points based on the final PCA carried out are presented below:

a) Sample size

Throughout the years many different propositions have been made in relation to what an appropriate sample size would be for a factor analysis leading to various “rules of thumb” being established. For example, 300 cases have been suggested as a probably adequate sampling size while others have recommended 100 cases as a minimum or on a ratio scale 5 to 10 cases per each variable to be measured (Field, 2000). In this pilot study there were 58 cases which is in line with the absolute minimum of 50 cases recommended by Hair (1998) and Habing (2003).

Nevertheless, being aware that this is still quite a small number of cases, the adequacy of the sampling size was also examined by various other methods that have been established and are easily measured in SPSS:

- i. Kaiser-Meyer-Olkin (KMO or else MSA) measures the sampling adequacy and even though ideally a value of 0.7 or above would be desired, the sample is considered adequate if KMO is above 0.5 (Field, 2000). In the present analysis, the final KMO was 0.627 thus meeting this criterion (Table 2.2).
- ii. Bartlett's Test of Sphericity is another measure of the strength of the relationship between variables and compares the correlation matrix with a matrix of zero correlations (Beaumont, 2012). As reported by Field (2000, p.457) “*it tests the null hypothesis that the original correlation matrix is an identity matrix*”, which would mean that there are no correlations between the variables and therefore a significant p value is required in order to be able to reject the null hypothesis. From the current analysis we can see that Bartlett's test of Sphericity is significant (Table 2.2) thereby justifying the conduct of a PCA.

Table 2.2

KMO and Bartlett's Test

Kaiser-Meyer-Olkin Measure of Sampling Adequacy		.627
Approx. Chi-Square		277.145
Bartlett's Test of Sphericity	Df	136
	Sig.	.000

b) Correlation Matrix

This is the starting point for all types of factor analysis and is consulted in order to assess whether we have appropriate correlations that would justify a factor analysis. In essence, PCA – like all other types of factor analysis – tries to combine variables together into factors (or

components) based on their correlations and therefore it is possible to form a first impression of what the factors will be by looking at the correlation matrix and identifying clusters of variables that are highly correlated between them. As a rule of thumb a substantial number of correlations is >0.3 otherwise there is no point in carrying on with the analysis since the variables are unrelated between them and thus cannot be modelled so as to form overarching factors (Tabachnick & Fidell, 2001).

Looking at the correlation matrix of this study (see Appendix 6) there are over 10 variables with a correlation above 0.3 thereby justifying continuation with the analysis.

b) Communalities

These figures show how much of the variance in each single variable has been accounted for by the extracted factors. The value ranges from zero to 1, where zero indicates that the variable cannot be predicted at all from any of the factors and 1 indicates that the variable can be fully defined by the extracted factors (Beaumont, 2012). Given that when carrying out a factor analysis it is hoped that the observed dataset will be reflected in the model being tested, a highest possible value is desired and the nearer to one it is, the better. In general it is accepted that the factor solution should explain at least half of each original variable's variance, so the communality value for each variable should be 0.50 or greater.

Looking at Table 2.3 below, we can see that for this study, all communalities were above 0.50 and 10 out of 16 were even above 0.7 indicating that they represent a significant amount of variability in the model.

According to Field (2000, p.43) communalities are also related to sample size and the lower they become the more important sample size is. Thus, if the communality is high the extracted factors account for a big proportion of the variable's variance and the sample size can be considered to be adequate, but if the communality is low, the sample size would have to be bigger in order to compensate for this. In terms of this study, there are many high communalities thus providing a further confirmation for the appropriateness of our sample size.

Table 2.3

Communalities

Questionnaire Items	Communalities
For me, having amniocentesis / CVS would be...(beneficial)	.617
For me, having amniocentesis / CVS would be...(reassuring)	.721
For me, having amniocentesis / CVS would be...(frightening)	.550
"I feel I have the tools to make decisions that will influence my future"	.757
"I feel I can make a logical evaluation of the various options available to me in order to choose one of them"	.730
"If it is offered to me, I think my partner will want me to..."	.744
"If it is offered to me I think my midwife/obstetrician will want me to..."	.591
The purpose of amniocentesis / CVS is to test for	.798
Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not	.832
I believe invasive diagnostic tests should never be done because they go against human nature	.701
For me, losing the current pregnancy through miscarriage as a result of amniocentesis / CVS would be...	.652
For me, giving birth to a child with a serious abnormality would be...	.583
In my opinion, chromosomal disorders such as DS would be the worst disability one could have	.728
"I feel I can make decisions that will change my family's future"	.798
"I find my partner's opinion about accepting or declining the test..."	.659
"I find my midwife's/obstetrician's opinion about accepting or declining the test..."	.738

c) *Initial number of components (factors) extracted*

The number of components that is initially extracted in PCA is exactly the same number as variables being analysed. In this case we had 16 variables being analysed and therefore 16 components were initially extracted. However, in general only the first one or two components can be expected to account for a fairly large amount of the total variance and each succeeding component will account for a progressively smaller amount of variance. Therefore, out of all the components initially extracted only the first few can be expected to be meaningful enough to be retained. The exact number can be assessed through various criteria discussed in the following section.

d) *Determining the number of meaningful components (factors) to be retained*

In PCA this decision can be facilitated through the following criteria:

- i. The eigenvalue-one criterion: This is also known as the Kaiser criterion (Kaiser, 1960) and is the most commonly used method in PCA in determining the number of factors

important enough to be retained for interpretation. The rationale is quite straightforward and begins from the assumption that each variable contributes one unit of variance to the total amount of variance.

According to this approach, any component with an eigenvalue over 1.00 is suitable to be retained and interpreted as this implies that it accounts for a greater amount of variance that has been contributed by one variable. On the contrary, any component with an eigenvalue that is less than 1.00 accounts for less variance that has been contributed by one variable and therefore should be ignored. To sum it up, the goal of PCA is to reduce the number of variables into a smaller amount of retained components which have an eigenvalue above 1.00.

Looking at Table 2.4, for this study there are 6 components with an eigenvalue over 1.00 and therefore these are the ones indicated for retention and interpretation. The Cumulative % is less than 100% because not all of the variance is explained when only some of the factors are retained in the final analysis. Components 7 through 16 were eliminated. Even though together they represent over 30% of the variance explained, any one of the factors accounts for very little variance and therefore is not considered significant enough to be retained.

The eigenvalue-one criterion is well-suited for the current study since it has been established as a reliable way of retaining the correct amount of components particularly when a small to moderate amount of variables are being analysed (<30) and communalities are above 0.70 (Stevens, 1986).

Table 2.4

Total variance explained

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	3.343	20.892	20.892	3.343	20.892	20.892
2	2.633	16.458	37.350	2.633	16.458	37.350
3	1.564	9.775	47.124	1.564	9.775	47.124
4	1.344	8.398	55.523	1.344	8.398	55.523
5	1.233	7.707	63.230	1.233	7.707	63.230
6	1.083	6.768	69.998	1.083	6.768	69.998
7	.833	5.207	75.205			
8	.697	4.357	79.562			
9	.680	4.249	83.811			
10	.620	3.872	87.683			
11	.453	2.830	90.513			
12	.437	2.732	93.245			
13	.333	2.080	95.325			
14	.302	1.888	97.213			
15	.239	1.496	98.709			
16	.207	1.291	100.000			

- ii. Proportion of variance accounted for: this indicates how much of the variability in the data can be accounted for by the extracted components. Most often researchers retain the amount of components that cumulatively account for a minimum accepted value, which is usually set to 60%, meaning that all the respective components put together explain 60% of the total variance (Beaumont, 2012). As observed in Table 2.4, the first 6 components in this study account for the 69.998% of variance and therefore are the ones that should be retained.

e) *Summary of basic criteria confirming the appropriateness of PCA*

As illustrated in Table 2.5, PCA is justified for our data-set and a total of 6 major components were identified.

Table 2.5

Summary of fulfilled criteria, confirming appropriateness of PCA for this study

GENERAL CRITERIA	PILOT STUDY
Number of minimum cases = 50	Number of valid cases = 58
Some correlations >0.30 (correlation matrix)	More than 10 variables >0.30
KMO \geq 0.50	KMO=0.637
Bartlett's test of sphericity must be significant	Bartlett's test of sphericity = .000
Eigenvalues > 1.0	6 eigenvalues > 1.0
Communalities > 0.50	All communalities > 0.50
Total variance explained > 60%	Total variance explained = 69.998%
No complex structure (no items with \geq 0.40 loadings on more than one factor – look at the pattern matrix)	No complex structure

f) *Giving meaning to the factors*

The next stage is to examine the variables that are grouped together under each of the extracted components in order to identify common themes.

One method that facilitates the process of interpretation is 'rotation', which aims to further analyse the extracted factors and make the factor loadings more transparent (Bountziouka & Panagiotakos, 2012). It is generally recommended as it simplifies the component structure and makes interpretation more reliable (Cattell, 1978). There are two types of rotation available in SPSS, but for the purposes of this study an *oblique* rotation was performed. Contrary to its alternative (*orthogonal* rotation), this method does not require components to be orthogonal to each other and thus allows variables to be correlated (Vogt, 1998).

Based on the results from the oblique rotation (see Appendix 7) the questions that load onto each of the six components are shown in Table 2.6.

Table 2.6

Breakdown of all extracted components

Breakdown of components extracted	Constructs measured
<u>Component 1:</u> "I believe invasive diagnostic tests should never be done because they go against human nature" "For me, having amniocentesis / CVS would be... (frightening)" "If it is offered to me, I think my partner will want me to..." "If it is offered to me I think my midwife/obstetrician will want me to..."	Attitude towards amniocentesis / attitudes towards having amniocentesis / subjective norms
<u>Component 2:</u> "I feel I can make decisions that will change my family's future" "I feel I can make a logical evaluation of the various options available to me in order to choose one of them" "I feel I have the tools to make decisions that will influence my future"	Perceived behavioural control
<u>Component 3:</u> "Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not" "For me, having amniocentesis / CVS would be... (reassuring)" "For me, having amniocentesis / CVS would be... (beneficial)"	Benefits of amniocentesis
<u>Component 4:</u> "I find my midwife's/obstetrician's opinion about accepting or declining the test..." "I find my partner's opinion about accepting or declining the test..." "For me, losing the current pregnancy through miscarriage as a result of amniocentesis / CVS would be..."	Willingness to comply with subjective norms / attitudes towards miscarriage as a result of amniocentesis
<u>Component 5:</u> "In my opinion, chromosomal disorders such as DS would be the worst disability one could have" "For me, giving birth to a child with a serious abnormality would be..."	Attitude towards chromosomal abnormalities
<u>Component 6:</u> "The purpose of amniocentesis / CVS is to test for..."	Knowledge

Looking at the breakdown of each of the above components (Table 2.6), it is clear that components 2, 3, and 5 are coherent and thus may represent a real-world construct. Components 1 and 4 however, include items that cannot logically be grouped together in order to form a coherent factor and thus should be removed from the questionnaire. Finally

component 6 only includes one question and will therefore also be removed as it is not strong enough to form a factor on its own.

This interpretation seems to reveal that, in reality, the original questionnaire (or at least the part that was subject to PCA) is composed of three subscales: *perceived behavioural control*, *benefits of amniocentesis*, and *attitudes towards chromosomal abnormalities*.

2.3. Internal reliability – Cronbach alpha

2.3.1. Background

Having decided to retain three components from the PCA based on a logical assessment of their respective items, a further statistical analysis – in the form of Cronbach α - was performed using SPSS, in order to confirm or challenge these conclusions.

Looking at the output generated in SPSS, the following three tables need to be consulted in order to draw conclusions:

a) “Reliability Statistics”

According to this table, a minimum value of $\alpha = 0.7 - 0.8$ is required in order for the respective scale to be considered to have a good internal reliability, thus indicating that all questions are measuring the same thing.

b) “Item-Total statistics: Corrected item – total correlations”

These values illustrate the correlations between each item and the total score retrieved from the questionnaire. In order for a scale to be considered reliable, all items must correlate with the total. Otherwise, if any of the items has a value less than 0.3 it might need to be dropped.

c) “Item-Total statistics: Alpha if item is deleted”

These values indicate the overall alpha value if each given question were to be removed from the calculation. Therefore, when reading this table we are looking for values that are greater than the overall alpha, because if the deletion of an item increases Cronbach alpha that means it improves the scale's reliability.

2.3.2. Internal reliability for each individual sub-scale produced by PCA

2.3.2.1. Subscale 1: Perceived behavioural control

This subscale appeared to have good internal consistency with $\alpha = .804$. In addition, all items are sufficiently correlated with the total (values greater than 0.6), while none of them would substantially affect reliability if they were removed (see Appendix 8). Therefore, all three items appear to be worthy of retention.

2.3.2.2. Subscale 2: Benefits of amniocentesis / CVS

Similarly this subscale had good internal consistency with $\alpha = .738$. All items were correlated with the total (values greater than 0.5) and none of them would increase reliability if they were to be removed (see Appendix 8). Therefore, all three items were suitable to be retained.

2.3.2.3. Subscale 3: Attitudes towards chromosomal abnormalities

Contrary to the other two constructs this subscale had a low internal reliability score with $\alpha=.466$ (see Appendix 8). This may be due to the fact that the specific sub-scale only consisted of two items which may not have been sufficient enough to measure what they set out to measure. According to Tavakol & Dennick (2011) "if the test length is short, the value of alpha is reduced". Therefore, they recommend that in an attempt to increase internal reliability, more items testing the same concept can be added to the test. This is a good point to be explored by future studies.

However, despite the low alpha score both items correlated with the total, meeting the threshold criterion of 0.3 and therefore at least for the purposes of this study this subscale will be retained as it is though results will be interpreted with cautiousness.

2.3.3. Internal reliability for other subscales included in the questionnaire

As previously mentioned, PCA was only performed on those sections of the questionnaire that were developed for the purposes of this study and needed to be assessed for their psychometric properties. However, there were other scales also included in the questionnaire that have previously been validated through other studies. Nevertheless, as it has been suggested to be good practice (Streiner, 2003) it was decided that a reliability test would also be applied to these individually in order to test for their suitability for this particular population (Streiner, 2003) (see Appendix 9).

a) Hospital Anxiety and Depression Scale (HADS) – Anxiety scale

This subscale seemed to have a lower level of internal reliability than expected, with $\alpha=.577$.

b) Attitude towards doctors and medicine

This subscale also had a low internal reliability based on this sample, with $\alpha=.601$

c) Health Locus of Control (HLOC)

Finally, this subscale also demonstrated low internal reliability for our sample, with $\alpha=.563$.

However, despite the low internal reliability scores for all three above scales, they will be retained in the questionnaire for the main study. Several previous studies have validated their psychometric properties and therefore the low alpha scores observed in this study may be more related to the size of the sample but may not be an issue in the main study where the sample will be significantly larger.

It is important to note here that the main purpose of this pilot study was mainly to assess those sections of the questionnaire that were newly developed, through the use of PCA and Cronbach alpha and thus the reliability of the latter three scales will again be assessed in the main study.

2.3.4. Questionnaire amendment based on PCA findings and cronbach alpha

All in all, based on the PCA the following factors will form part of the amended version of the questionnaire (see Appendix 10) to be used in the main study together with the previously validated scales mentioned in 2.3.2 above.

A detailed account of all factors included in the original and the amended questionnaire is illustrated in Table 2.7. The amended questionnaire will be referred to as Prenatal Decision Making Questionnaire (PDMQ) for the remainder of the study.

Table 2.7

Factors included in the original and the amended questionnaire			
Original questionnaire		Amended questionnaire (PDMQ)	
1. Knowledge		1. Perceived behavioural control	
2. Attitude towards amniocentesis / CVS		2. Benefits of amniocentesis / CVS	
3. Attitude towards having amniocentesis / CVS		3. Attitudes towards chromosomal abnormalities (burden attached)	
1. Attitude towards miscarriage as a result of amniocentesis / CVS		4. Anxiety (HADS – anxiety scale)	
2. Anticipated decision regret		5. Attitudes towards doctors and medicine	
3. Attitudes towards chromosomal abnormalities (burden attached)		6. Health Locus of Control (HLOC)	
4. Perceived risk of having a child with a chromosomal abnormality			
5. Perceived behavioural control			
6. Subjective Norms			
7. Anxiety (HADS – anxiety scale)			
8. Attitudes towards doctors and medicine			
9. Health Locus of Control (HLOC)			

2.4. Preliminary findings based on pilot study sample

Basic statistical tests were conducted on the pilot study population in order to get some more information on the sample and gauge women's responses thus far on the variables being measured.

2.4.1. Sample characteristics

The vast majority of participants were white (75.7%) while various minority groups made up the rest of the sample (see Table 2.8). In terms of religion, 58.6% of the total sample was Christian while quite a large amount was of 'no religion' (36.2%). This is in line with national data that indicate a steady increase in the amount of adults who are living in the UK and reporting they have 'no religion', with numbers rising from 47% in 2001 to 59% in 2009 (Office for National Statistics, 2013). The sample was almost equally divided into women under the age of 35 (55.2%) and women aged 35 or over (49.8%), while the mean age for the total sample was 33.67 (minimum: 23; maximum: 45; *SD*: 4.940). This is slightly higher than the national average that was reported to be 30 years of age in 2013 (Office for National Statistics, 2013). However, looking back at previous years, there has been a steady increase in the mean age of women at childbirth rising from 27.9 in 1993, to 28.8 in 2003 and 29.3 in 2008, suggesting that the last reported figures from 2013 may have increased as well reaching more towards our own sample characteristics. What is more striking, however, is the division in age groups with national averages reporting that 78.99% of live births in 2013 were to women aged 20-34 and the remaining 21.01% to women aged 35 or over (Office for National Statistics, 2013). This is something worth keeping in mind when considering the more equal distribution in our sample.

The vast majority of women (94.8 %) in our sample were either married or living with their partner at the time of the survey which also contradicts the reported national average of 52.6% of live births being to married couples. However, it must be noted that we included couples living together regardless of being married or not in this category and therefore this may justify the seemingly big difference between our and the national findings without necessarily representing a true difference. The majority of the sample (67.2%) had an annual household income of £35,001-150,000 and overall the participants were of a varied educational background (see Table 2.9) with 81.1% having a university degree of some level.

Table 2.8

Breakdown of participants' ethnic origins

Ethnic group	Percentage
White (British or other)	75.7%
Black (British or other)	8.5%
Asian (British or other)	3.6%
Chinese	3.6%
Mixed	6.8%

For the 84.5% of the sample this was a planned pregnancy. This is in line with reports from the NATSAL study (Mercer et al, 2013) whereby 1 in 6 pregnancies in Britain are unplanned, translating into 84% being planned. Out of the total sample, the 15% reported having difficulties in getting pregnant with the 3.4% having had to be assisted by IVF in order to conceive. The 25.9% of the sample had had a previous miscarriage whereas the 20.7% reported having had a termination of pregnancy in the past. Finally, only 3.4% of the participants reported having had an invasive test in the past and 32.8% reported that they knew of someone close to them having undergone such a procedure.

Table 2.9

Participants' level of education

Level of education	Percentage
Secondary School	13.8%
University degree	48.3%
Postgraduate studies	32.8%

2.4.2. Preliminary findings for the variables being studied

In an attempt to get a first impression on how women scored in the variables that were retained following the Principal Component Analysis, descriptive statistics were conducted appropriately.

The total sample consisted of participants that showed varying degrees of anxiety levels according to the HADS-anxiety scale measurements (see Table 2.10). It is important to note that almost half of the sample (48.3%) reported quite elevated anxiety levels indicating that they may be in need of support at this point in order to help alleviate their stress and not interfere with a healthy pregnancy. This is in line with previous studies reporting elevated levels of

anxiety in approximately 1 in 2 women, and this being the case during the first and third trimester as opposed to the second trimester which seems to be less stressful (Lee, Lam, Lau, Chong, & Fong, 2007).

Table 2.10

Assessment of anxiety levels based on the HADS scale	
Diagnosis based on anxiety levels	Percentage
Non-case	51.7% (n=30)
Borderline case	32.8% (n=19)
Case	15.5% (n=9)

In terms of attitudes towards doctors and medicine, the findings were contradictory. Participants demonstrated a slightly more negative attitude towards doctors but appeared to be more positively inclined towards medicine (see Table 2.11). While this was not further explored, it may be due to women's past experiences with doctors or even simply down to associating their doctors with the communication of potentially painful information and thus creating a negative feeling. On the other hand, medicine and any relevant medical test may be viewed as a useful source of information / intervention thus creating a more positive attitude.

Table 2.11

Scores for attitudes towards doctors and medicine scales

Scores	Attitude towards doctors		Attitude towards medicine	
	Positive	Negative	Positive	Negative
Mean	11.16	12.47	13.17	12.36
SD	(2.36)	(2.99)	(2.38)	(2.33)

According to the Health Locus of Control Scale, 70.7% of the total sample indicated a greater *internal* locus of control, with 13.8% scoring high on the *chance* locus of control, and 8.6% scoring high on the *powerful others* dimension. This is an encouraging finding as it is thought that those who believe they have some degree of control are more likely to take responsibility for their actions and make more informed choices.

Likewise, 91.4% of the sample demonstrated high levels of perceived behavioural control which again leads to the assumption that they feel they are in a position to take control of their and their baby's health and any decisions related to it.

With regards to attitudes towards chromosomal abnormalities the majority of the sample (58.6%) reported these to be negative compared to the 39.7% that reported a more positive attitude towards chromosomal abnormalities.

Finally, 69% of participants scored high on the perceived benefits of amniocentesis / CVS scale, indicating a potentially strong factor that would influence them towards having the test.

2.5. Power analysis – calculating the sample size for the main study

2.5.1. Background

The starting point for any research is setting a null hypothesis and subsequently performing the relevant statistical tests in order to determine whether this can be accepted or not. For example, in this particular study the null hypothesis could be that *“there is no difference in the mean outcome measure for all variables under study between women who decide to have amniocentesis and women who decide not to”*. Ideally, we would like to be able to reject the null hypothesis and to show through statistical procedures that the different outcome decision between the two groups of women is not a result of chance. Once the null hypothesis has been determined, it is important to look at other constructs that will enable this process along the way.

The Central Office for Research Ethics Committees (2007) has proposed some guidelines emphasising the importance of calculating the appropriate sample size, according to which *‘the number should be sufficient to achieve worthwhile results, but should not be so high as to involve unnecessary recruitment and burdens for participants’*. Therefore, in order to maintain a balance and for studies to neither be underpowered (too few participants) nor overpowered (too many participants), it has become common practice for researchers to calculate the sample size that will be sufficient to achieve adequate power to carry out planned hypothesis testing (MacCallum, 1996).

2.5.2. Calculating the sample size

Sample size (n) is in essence a function of three factors – the significance level, power, and effect size. Thus, in prospective studies the most common practice is to calculate n , using a conventional level of significance, effect size and a desirable power (McCrum-Gardner, 2010).

a) Significance level (p value).

This is the probability cut-off which is chosen prior to performing the test, and usually a value of $p=0.05$ (or $p=0.01$) is used (Erdfelder, Faul, & Buchner, 1996). However, this is not absolute and it depends on how much safeguard is required against accidentally rejecting the null hypothesis when it is actually true.

b) Effect size.

This is a measure of the difference in the outcomes between two or more groups, and is the smallest difference that is considered to be clinically relevant (Prajapati, Dunne, & Armstrong, 2010; McCrum-Gardner, 2010). While there are numerous ways for this to be calculated, Cohen

(1962) through his work on the power of statistical tests in behavioural research, established some standardised effect sizes which he characterised as 'small', 'medium', and 'large'. Following an extensive study on effect size in social psychological research, and Cooper & Findley's (1982) conclusion that it is reasonable to assume a medium effect size in power analysis, the majority of power studies observed in the literature have indeed used Cohen's definitions as a guide (Sedlmeier & Gigerenzer, 1989).

c) Power.

This represents the type II or beta error probability of falsely retaining an incorrect H_0 (Faul, Erdfelder, Buchner, & Lang, 2009). In other words, the statistical power of a test ($1-\beta$) measures its ability to reject the null hypothesis when it should actually be rejected. As a rule of thumb, 80% is considered as the minimum accepted level meaning that there is a 20% chance of accepting the H_0 in error ($\beta=20\%$). It is easily assumed that studies that lack statistical power are of limited use as they do not allow safe conclusions to be drawn in relation to the discrimination of the H_0 from the alternative hypothesis (H_1).

2.6. G power 3.1 – Analysis and results

The importance of statistical power analysis for every research study in the social, behavioural, and biomedical sciences is widely reported in the literature and several authors have provided extensive tables of power and relevant sample sizes (Erdfelder et al, 1996). However, it was not until the late 1980's that power charts (Scheffe, 1959) and power tables (Cohen, 1962) were replaced by more precise, efficient, and user-friendly computerised power analysis programs (Goldstein, 1989).

One such application that was also used for the purposes of the present pilot study is the programme Gpower (version 3.1) which is freely available online (<http://www.psych.uni-duesseldorf.de/abteilungen/aap/gpower3/download-and-register>) and is commonly used for numerous statistical tests in the social, behavioural, and biomedical sciences (Faul et al, 2009).

All in all, there are three steps in this application:

a) Selection of statistical test to be used

G power 3.1 offers a wide variety of statistical tests including: one sample correlation tests; statistical tests comparing both dependent and independent Pearson correlations; simple linear regression coefficients; multiple linear regression coefficients for both fixed- and random-predictor models; logistic regression coefficients; and, Poisson regression coefficients (Faul et al, 2009).

In this case t-tests were computed using the statistical software Gpower 3.1 in order to determine the required sample size for the comparison between three independent groups: women choosing to have an invasive diagnostic test, women choosing NIPT, and women choosing to have no further testing at all.

b) Specification of the desired type of power analysis

Depending on the phase of the research and the research question, G power 3.1 offers the following five types of power analysis: A priori analysis; Post hoc analysis; Compromise analysis; Criterion analysis; and, Sensitivity analysis.

For the purposes of the current study an *a priori* type of analysis was performed as this is the most relevant and efficient method for sample size calculation (Prajapati et al, 2010). One of its strongest points is that it allows for statistical power, alpha level and effect size to be controlled prior to the study being conducted (Hager, 2006) while the respective values can be determined by the researcher without any restrictions.

c) Selection of the accuracy level of the calculations

In line with conventional values found across the literature, for the present analysis a power of 0.80 was used, alongside a medium effect size (0.5) according to Cohen's measurement standards, and a significance level of .05. A two-tailed test was also selected as it is unknown towards which direction the two groups will differ between them.

Based on the aforementioned specifications it was found that a sample size of 159 participants will be required for the main study in order to have sufficient statistical power and draw safe conclusions about the decision-making factors that influence women in having an invasive test or not (see Figure 1).

F tests – ANOVA: Fixed effects, omnibus, one-way				
Analysis: → A priori: Compute required sample size				
Input:	→	Effect size f	→	=→0.25
	→	α err prob	→	=→0.05
	→	Power (1 - β err prob)	→	=→0.80
	→	Number of groups	→	=→3
Output:	→	Noncentrality parameter λ	→	=→9.9375000
	→	Critical F	→	=→3.0540042
	→	Numerator df	→	=→2
	→	Denominator df	→	=→156
	→	Total sample size	→	=→159
	→	Actual power	→	=→0.8048873

Figure 1. G power analysis parameters for calculation of sample size for the main study

2.7. Target population for the main study

As with the pilot study, the target population for the main study will consist of pregnant women attending King's College Hospital (KCH) for their first trimester combined screening test. Prior to receiving their screening results women will be given the questionnaire to complete if they wish

to participate in the study. Other inclusion criteria involve age 18 or over, ability to read and write English, and absence of any mental illness at the point of data collection.

2.8. Conclusion

Adopting a holistic approach and through a comprehensive combination of key psychological models and literature evidence, a questionnaire was developed aiming to explore pregnant women's decision making factors when it comes to the uptake of invasive testing.

Overall, the questionnaire consisted of some scales that have previously been validated through several studies and have been reported to have good psychometric properties. However, for a number of factors to be explored no measures were identified in the literature and thus new scales were developed for the purposes of this study. Therefore, the present pilot study was conducted with a main goal to validate these scales before proceeding to the main study.

A Principal Component Analysis (PCA) was performed using SPSS and this was followed by a reliability test, namely Cronbach alpha using the same statistical software. As a result, the following three valid components were formed: *perceived behavioural control*, *attitude towards chromosomal abnormalities*, and *benefits of amniocentesis / CVS*. Therefore only their respective questions were retained and the rest were dropped as there was no evidence of their contribution to the questionnaire.

This lends support to the initial assumption that a combination of different variables from different theoretical models can actually be construed into an integrative approach to predicting one's decision (Shiloh, 2006) although it was still disappointing to not be able to measure the role of all the variables we set out to explore. Out of the different psychological models that informed the development of the questionnaire it can be seen that some constructs were not supported, leading to various interpretations on how clear-cut each of the models used is and offering encouraging evidence for the flexibility in which these can be used in order to formulate a more efficient predictive model.

More specifically, Ley's Cognitive Hypothesis (1989) whereby those deciding to have a procedure (i.e. amniocentesis / CVS) will have greater knowledge of the test than those not undergoing it, was not supported by this questionnaire, adding more controversy to the current literature findings (French, Kurczynski, Weaver, & Pituch, 1992). In terms of this specific variable a possible explanation may be that actually the group of participants in this pilot study were mostly low-risk women and thereby were not actually faced with a decision to have an invasive test or not, so knowledge about it may not have been that relevant to their responses as they may have not felt the need to find out about the test before they actually "have" to consider it. Another potential explanation is that there were not enough items exploring 'knowledge' about the test and therefore, if more questions were added this could have led to a different outcome.

Likewise, the subjective expected utility model (Savage, 1954) was not fully supported by this questionnaire. This model posits that an individual will base their decision on an assessment of their subjective outcomes of a behaviour (in this case weighing costs and benefits of amniocentesis / CVS) and their own subjective risks associated with that behaviour (i.e. how likely they are to have a baby with a chromosomal abnormality such as Down's syndrome). In other words, similarly to the Health Belief Model (Rosenstock, 1966) it is hypothesised that one will weigh up the costs and benefits of undergoing a diagnostic procedure (i.e. amniocentesis / CVS) in relation to their perceived susceptibility to conditions tested for by that procedure (i.e. Down's syndrome) (Mongin, 1997). However, based on the principal component analysis results for this questionnaire it appears that while benefits of amniocentesis / CVS were significant enough to form an influential factor in women's decision making process, the costs associated with it and women's perceived susceptibility to certain conditions were not prominent enough to form distinct factors in this process. Furthermore, perceived severity of chromosomal abnormalities such as Down's syndrome was not relevant to this questionnaire, meaning that the only variable retained from the HBM were 'benefits of amniocentesis / CVS'. This again, can possibly be interpreted as women mainly focusing on the benefits of amniocentesis / CVS when considering a hypothetical scenario of them being faced with such a decision. However, as these women were mostly low risk it is not possible to draw any further conclusions as to whether this indeed leads them to have the test or whether they can acknowledge the value of the test regardless of whether they decide to undergo it or not. This is a point for further exploration with a population where women of medium to high risk are actually faced with this decision, but is beyond the scope of this study.

Another model that was partially supported by this questionnaire was the Theory of Planned Behaviour (TPB; Ajzen, 1988). In line with this theory, it seems that women's attitudes towards chromosomal abnormalities such as Down's syndrome were quite prominent in this questionnaire and the items generated were powerful enough to form a factor. It is interesting that attitudes towards the actual behaviour of undergoing invasive testing were not reflected as a valid factor in this questionnaire but this may have been due to the limited number of items referring to this variable rather than it not being influential in women's decision. Likewise, 'subjective norms' were not supported by this questionnaire, although once again it is uncertain whether this is because women are not that influenced by others in their decision or whether the addition of further items might have led to the formation of such a factor. However, upon reflection, a similar scale that was used in an earlier study (Van den Berg, 2008) had a low internal reliability ($\alpha=0.59$) suggesting that indeed the influence of others may not be that central in the decision making process of invasive testing. However, 'perceived behavioural control' was sufficiently represented in this questionnaire indicating the importance of empowering women to make their own decisions and take control of their lives and wellbeing. This is supported by previous findings whereby perceived behavioural control predicted participation in cancer screening (Devellis, Blalock, & Sandler, 1990), and other health protective behaviours such as attending routine health screening (Conner & Norman, 1994) and condom use (Fisher, 1984). However, even though a methodological limitation of most previous studies is that they

measure intentions of performing a behaviour that has been previously performed and thus the prior experience of performing this act is indeed the strongest predictor of intention and behaviour (Sutton, 1994), a study exploring a novel behaviour also reported perceived behavioural control to be a significant predictor of women's intentions to take hormone replacement therapy for the first time (Quine & Rubin, 1997). This strengthens the findings of our study where women may not have necessarily had a previous pregnancy and therefore are more likely to be faced with prenatal diagnostic decisions for the first time yet this not compromising the role of perceived behavioural control.

Interestingly, contrary to prior evidence the previously validated scales included in the questionnaire – *HLOC*, *Attitudes towards doctors and medicine*, and *HADS (anxiety scale)* – were found to have low internal reliability for this specific sample. However, this is likely to be due to the rather limited sample size and thus will not affect their inclusion in the main study where the sample size will significantly be increased.

To sum up, the final questionnaire (PDMQ) that will be used in the main study consists of a combination of various theoretical constructs examining the following factors for their contribution to women's decision making process regarding the uptake of invasive testing: *benefits of amniocentesis / CVS*, *perceived behavioural control*, *attitudes towards chromosomal abnormalities*, *Health Locus of Control*, *attitudes towards doctors and medicine*, and *anxiety*.

3. Chapter Three: Main Study

3.1. Background and current practices

According to guidelines by the National Screening Committee, the current standard screening procedure in the National Health System (NHS) in the UK is the first trimester combined test which incorporates fetal ultrasound and maternal serum biomarkers (NSC, 2015). The benefit of this test is that it detects approximately 90% of foetuses with trisomy 21 (T12) and 95% of fetuses with trisomies 18 and 13 (T18/T13), although its limitation is that it entails a 5% false positive rate (FPR) (Nicolaidis, 2011). This combined test is typically offered to all pregnant women and provides an individualized risk estimate. Women who are identified as high risk ($\geq 1:150$) are then offered the option of an invasive diagnostic test either in the form of Chorionic Villus Sampling (CVS) from 11 weeks of gestation or amniocentesis from 15 weeks (Alfirevic, Gosden, & Neilson, 2000). However, while both these tests provide a definitive diagnosis, they also entail up to 1% risk of miscarriage (Tabor & Alfirevic, 2010).

An alternative, non-invasive method for risk assessment (NIPT) was first suggested in the late '90s following the discovery of cell-free foetal DNA (cffDNA) in the maternal blood stream (Lo et al, 1997). While there were initial difficulties in distinguishing the foetus-specific genetic information from the maternal cell-free DNA, recent advances in technologies have helped overcome this obstacle and large clinical trials have validated the ability of non-invasive prenatal testing (NIPT) in detecting foetuses affected by Down's syndrome (T21) as early as 10 weeks into the pregnancy with a detection rate of 99% and a low FPR of 0.1%. Detection rates are also high for T18 (96%) and T13 (92%) (Gil, Akolekar, Quezada, Bregant, & Nicolaidis, 2014). While NIPT is more accurate than the conventional combined screening test, it still entails a small percentage of false positive (FP) and false negative (FN) results and is therefore considered a highly sensitive screening tool rather than a diagnostic test (Nicolaidis et al, 2012), with results requiring confirmation via invasive tests that provide a definitive diagnosis (ACOG, 2012).

When considering the advantages of NIPT, the two most frequently cited are the absence of procedure-related risk of miscarriage and the attainment of results early on in pregnancy (Lewis, Choudhury, & Chitty, 2014). While these are undoubtedly of clinical significance, the limitations of NIPT should also be taken into account when comparing to invasive testing (IT). Firstly, in its current form NIPT is only accurate in detecting the three main chromosomal abnormalities, T13, T18, and T21 whilst failing to detect the majority of other genetic conditions that are identified through invasive testing (Nicolaidis, Syngelaki, Gil, Atanasova, & Markova, 2013). Even though efforts to expand the range of detectable conditions via NIPT, including sub-chromosomal abnormalities, are already being reported (Srinivasan, Bianchi, Huang, Sehnert, & Rava, 2013) these are in their early stages and large clinical trials remain to be conducted before further conclusions can be drawn (Vora, & O'Brien, 2014). In addition, there is a margin of 5% out of the total NIPT cases that produce inconclusive results; while this may be

due to a number of reasons it is most often due to a low foetal fraction (Gil, Giunta, Macalli, Poon, & Nicolaides, 2015) or an increased maternal BMI (Wang et al, 2013).

Furthermore, as a result of the ease with which NIPT is offered via a simple blood draw and the absence of any risk may also incur potential additional drawbacks. Building on pre-existing ethical debates as to women's difficulty to choose to reject technologies approved by their obstetricians (Wertz & Fletcher, 1993) women have already expressed concerns of feeling more pressured into accepting the test and less justified in declining it (Lewis, Silcock, & Chitty, 2013). In addition to this, and in light of recent evidence supporting its effectiveness not only in high risk but also in low risk pregnancies (Nicolaides et al, 2012), it is likely that NIPT will be offered routinely as part of standard antenatal care. This is likely to jeopardise informed consent, as it is likely that women will be offered the option of NIPT without appropriate genetic counselling beforehand; up until the introduction of NIPT women undergoing their 1st trimester combined screening test were offered minimal information about the genetic abnormalities detected and the subsequent steps they would have to take to confirm a high-risk indication and were only provided with further information should they be classified as being at high risk (Benn & Chapman, 2010). While this served to protect low risk women from unnecessary emotional disturbance and also catered to the limited availability of genetic counsellors, in the event of a NIPT it may pose greater danger as women may be proceeding without realising the potential outcomes and the gravity of the decisions they may then be faced with. However, in the absence of risk they are more likely to undergo such a blood test and thus potentially may be setting themselves up for a more distressing experience having not given the appropriate consideration to all factors in advance (Schmitz, Henn, & Netzer, 2009). Nonetheless, despite the apparent simplicity of NIPT, at the end of it women are likely to be faced with life-changing decisions such as terminating or continuing with their pregnancies (following confirmation via an invasive test) and therefore it is of utmost importance for the informed decision process to remain a priority during implementation of any structural changes in prenatal testing.

Following the volume of evidence in support of the effectiveness of NIPT it is now available in the private sector in numerous countries and discussions are centered on ways of implementing it in the public sector (Everett & Chitty, 2014). Considering the current prenatal testing policies within the NHS there have been several propositions so far: NIPT could either replace the standard combined screening test at 11-13 weeks of gestation and be routinely offered to all pregnant women, or alternatively it could replace invasive testing although there are reservations in this area due to its small but significant false-positive rates (Lewis et al, 2014). The final and most likely and cost-effective suggestion so far is for NIPT to be used as a contingent screening for women who are identified as moderate-high risk through the 11-13 week test (Gil et al, 2014). This would lead to very high detection rates, whilst also maintaining the advantages of the combined screening through ultrasound and biochemistry, consequently minimising the number of confirmatory invasive tests required and the associated procedure related miscarriages (Nicolaides, Syngelaki, Poon, Gil, & Wright, 2014).

Preliminary findings suggest that the introduction of NIPT has already had a significant impact on foetal medicine practice so far as indicated through a marked reduction in invasive tests (Ferres, Lichten, Sachs, Lau, & Bianchi, 2014). More specifically a UK study reported a 26% decrease in the rate of invasive tests requested by high-risk women and a 94% decrease in women who would have previously rejected invasive tests but who now opted for the NIPT (Gil et al, 2015).

With the imminent wider implementation of NIPT through its incorporation in the public health system, it is important to consider the factors that affect women's decision to have an invasive test, non-invasive or no test at all. While some such studies have been carried out in relation to invasive testing and even more so in relation to screening, due to the fairly recent introduction of NIPT in prenatal testing, studies are only now starting to explore the decision making process addressing this new addition. Overall, preliminary evidence suggests an overwhelmingly positive response of women to non-invasive testing as it would offer safe, early, and accurate results (Hill, Fisher, Chitty, & Morris, 2012). This finding was also supported by a more recent clinical trial where NIPT was introduced as a contingent to the routine antenatal screening in an NHS hospital and found that within the high risk population most women chose NIPT instead of invasive tests and within the intermediate risk population NIPT was chosen by more than 90% of the patients (Gil et al, 2015). Nonetheless, considering the disparity in women's choices including a small yet significant portion of women who continue to refuse any kind of testing (Allyse, Sayres, Goodspeed, & Cho, 2014) it is important to look into the factors that influence this decision and identify any different patterns between the groups so as to be able to provide relevant support during this challenging process.

3.1.1. Aim of this study

Using the questionnaire that was developed and pilot-tested for the purposes of this study (Appendix 10), the aim was to identify the factors that mostly influence uptake of prenatal diagnostic testing, including NIPT. As described in more detail in Chapter 2, the following factors were included in the questionnaire: Perceived Behavioural Control; Attitudes towards prenatal testing; Attitudes towards chromosomal abnormalities; Attitudes towards doctors and medicine; Health Locus of Control; and Anxiety. In addition, the role of socio-demographical factors, family and medical history, were also explored in terms of their role in the decision making process.

3.1.2. Study Hypotheses

The hypotheses are as follows:

- Women with an increased sense of behavioural control will be more likely to opt in for further testing whether invasive or non-invasive.
- Women with a positive attitude towards prenatal testing will be more likely to opt in for further testing whether invasive or non-invasive.

- Women with a positive attitude towards chromosomal abnormalities will be more likely to opt in for further testing whether invasive or non-invasive.
- The more positive the attitude towards doctors and medicine the more likely that these women will opt in for further testing whether invasive or non-invasive.
- Women with a greater internal or powerful others locus of control will be more likely to have further testing whereas women with a greater chance locus of control will be more inclined towards no further testing.
- The role of anxiety and other socio-demographical and family/medical history factors was also explored in relation to the decision-making process.

3.2. **Methods**

3.2.1. **Sample**

Women attending for their first trimester combined screening test were approached to participate in this study prior to finding out their risk status for carrying a baby with a chromosomal abnormality such as Down's syndrome. As with the pilot study, the inclusion criteria included women aged 18 or over, the ability to comprehend English language, and absence of any mental health conditions which were assessed through a screening tool incorporated in the questionnaire.

3.2.2. **Materials**

The questionnaire (PDMQ) that was used in this study comprised of the following sub-scales:

a) Anxiety (HADS; Zigmond & Snaith, 1983).

This consists of seven items scored on a Likert-type scale (0-3) and total scores range from 0 to 21. The higher the score the greater the level of anxiety. It has been used extensively in clinical and non-clinical populations and has good psychometric properties, with a reported specificity of 0.78 and sensitivity of 0.9 (Bjelland, Dahlb, Haug,&Neckelmann, 2002).

b) Multidimensional Health Locus of Control Scale – Form A (MHLC; Wallston & Wallston, 1978).

This consists of 18 items scored on a 6-point Likert type scale (1=Strongly Disagree, 6=Strongly Agree). It comprises of three further sub-scales, namely Internality (IHLC) which measures the extent to which one believes they have control over their own health; Powerful Others externality (PHLC) which measures how much one believes that powerful others such as physicians or other health professionals control their health; and, Chance externality (CHLC), which measures how much one assigns their health to luck, fate, or chance. Each participant is scored on each of the three sub-scales that are interpreted as follows: a score of 23-30

indicates a strong inclination towards that particular subscale; a score of 15-22 indicates a moderate inclination and a score of 6-14 indicates a low inclination towards that subscale.

c) Attitudes to doctors and medicine (ADMS; Marteau, 1990).

This measure which was developed and tested on an antenatal population consists of the following four subscales that were found to be of good internal reliability: Positive Attitudes towards Doctors (cronbach α =0.76); Negative Attitudes towards Doctors (cronbach α =0.67); Positive Attitudes towards Medicine (cronbach α =0.67); and, Negative Attitudes towards Medicine (cronbach α =0.61). Items are scored on a 5-point Likert type scale (1=strongly disagree, 5=strongly agree)

d) Perceived Behavioural Control.

This scale was developed for the purposes of this study and consists of three items scored on a 5-point Likert type scale (1=Strongly Disagree, 5=Strongly Agree). It was pilot tested on our target population of women attending for their first trimester screening test and had a good internal reliability (Cronbach α =.804).

e) Attitudes towards prenatal testing.

This scale which consists of 3 items scored on a 5-point Likert type scale was also developed for the purposes of this study and was found to have good internal reliability through the pilot test conducted on our target population (Cronbach α =.738).

f) Attitudes towards chromosomal abnormalities.

This scale consisting of two items and scored on a 5-point Likert type scale was developed for the purposes of this study and contrary to the previous two was found to have a low internal reliability (Cronbach α =.466). Nonetheless, this is probably due to the limited number of items and it was therefore decided to include it in the current study.

g) Screening Tool.

A brief screening measure for mental health issues was developed for the purposes of this study. This included a mixture of ten health-related issues covering both, mental health, such as depression and schizophrenia, and common health problems, such as migraine and allergies. The aim of the common health problems was to slightly mask the emphasis on asking questions just about mental health. Participants were also asked to state any medication they were taking at the time. The purpose of this screening tool was to allow for exclusion of those who were suffering from any sort of mental health issue, which may have impacted on their responses to the other scales of the questionnaire.

3.2.3. Procedure

All women attending for their first trimester combined screening test at King's College Hospital (KCH) between the months of September 2014 and January 2015 were approached to participate in this study. At the end of their screening procedure their sonographer briefly informed them of the purposes of this study and handed them a pack that included the questionnaire (Appendix 10), a participant information sheet (Appendix 15), a consent form (Appendix 16), and a debrief sheet (Appendix 17). Incentives were also used as a means to encourage participation, and included a free packet of Pregnacare supplement tablets with each questionnaire and a prize draw that would be taking place at the end of the study and which would automatically include all women who had participated in the study, with a prize of a £200 voucher to be spent in a big retailer chain-store that specialises in products for expectant mothers and general merchandise for new-borns and children up to 8 years old. Women who were interested to participate were given the option to either return the questionnaire via post using the enclosed pre-paid envelope or by handing it back to their medical team.

3.2.4. Statistical Analysis

The statistical programme SPSS version 21 was used to compute the descriptives of our sample, cross-tabulations of variables and mean comparisons. R version 3.0.3 was used to perform the logistic regressions.

The normality of the data was explored using the excess skewness and excess kurtosis statistics. Several researchers have suggested an acceptable limit of +2 for the excess (Trochim & Donnelly, 2006; Field, 2000; Graviter & Wallnau, 2014). We used the parametric t-test to compare the mean levels of the predictors (PAD, NAD, and Chance locus of control) and the non-parametric equivalent Mann-Whitney U test for the rest of the predictor variables (anxiety, PAM, NAM, Internal locus of Control, etc.) for the low vs. intermediate/high risk groups. Equality of variance (homogeneity) between the groups was assessed using Levene's test and where the homogeneity was rejected, the Welch t-test statistic will be reported (Ruxton, 2006). The non-parametric Kruskal Wallis test (equivalent of ANOVA) was used for the comparison of mean level of predictors across the low vs. intermediate vs. high risk group due to the highly unequal sample sizes. We furthermore assessed the effect size differences in the mean scores of Amnio/ CVS vs. no test and NIPT vs. no test, using Cohen's D effect size.

The penalised maximum likelihood estimations were used for the regression model as proposed by Firth (1993) as well as the methodology proposed by King (2001) since the likelihood of selecting an Amnio/ CVS test was rare (4 women out of 414 - 0.97%). The two methods correct the bias in the coefficient estimations, a problem usually seen in the study of rare events. Therefore they will essentially produce more accurate estimates of the effect of different factors in the event under consideration (uptake of an invasive test). The Akaike AIC was used to compare the goodness of fit of the two regressions (Venables, 2002). The R

packages used were *logistf*¹ for the Firth logistic and *relogit*² for the Kings methodology. The *logistf* and *relogit* were also used for the logistic regression of the Harmony vs. No test model since the problem of separation (Harmony 36.8% vs No test 63.2%) also existed (Heinze, 2006).

3.3. Results

3.3.1. Overall description

Overall, 421 questionnaires were collected but with four participants providing incomplete data the total sample comprised of 417 participants (N=417). Table 3.1 provides a summary of the decision outcome in relation to whether participants decided to have an invasive test (CVS), NIPT or no further test, which also represents the output measure for this study.

Table 3.1

Summary of decision outcome for the overall sample (N=417)

DECISION OUTCOME	NUMBER OF PARICIPANTS	(%)
Invasive test (CVS)	4	(1%)
Non-invasive prenatal test (NIPT)	151	(36.2%)
No further test	262	(62.8%)
TOTAL SAMPLE (N)	417	(100%)

In order to gain further insight to factors that affected the decision outcome this was examined in relation to risk status for T21 (Down's syndrome) and separately in relation to risk status for T13 (Patau's syndrome) / T18 (Edward's syndrome). This was based on the fact that following their combined screening test women are provided with two separate results representing a risk status for T21, and a risk status for T13/T18 which are grouped together. It is likely that depending on the identified genetic condition women's decisions may differ and therefore such an exploration may provide useful information (Verweij, de Boer, & Oepkes, 2014). However, due to a further three missing cases where the decision outcome was not reported the final sample comprised of 414 participants (N=414). Table 3.2 and Table 3.3 illustrate women's decision outcomes in relation to risk status for T21 and T13/T18 respectively.

¹<http://cran.r-project.org/web/packages/logistf/index.html>

²<http://zeligproject.org/>

Table 3.2

Decision outcome depending on risk status for T21 (Down's syndrome)

RISK STATUS (n)	CVS	NIPT	No Test	Number of participants (n) per group (%)
Low	0	9	254	263 (63.5%)
Intermediate	0	134	5	139 (33.6%)
High	4	8	0	12 (2.9%)
Total	4	151	259	N=414 (100%)

Table 3.3

Decision outcome depending on risk status for T13 (Patau's syndrome) / T18 (Edward's syndrome)

RISK STATUS (n)	CVS	NIPT	No Test	Number of participants (n) per group (%)
Low	0	99	258	357 (86.2%)
Intermediate	4	49	1	54 (13%)
High	0	3	0	3 (0.7%)
Total	4	151	259	N=414 (100%)

Further tests were then conducted to identify women who are either low risk on both T21 and T13/T18 or have some element of risk (intermediate or high) on either one or both of the conditions (Table 3.4).

Table 3.4

Women's risk status across conditions (T21 vs. T13/T18)

Risk status across conditions	Number of participants (%)
Low – Low (low risk on both T21 and T13 / T18)	253 (61.1%)
Low – Intermediate (low risk on one of the two conditions and moderate risk on the other)	109 (26.3%)
Low – Intermediate (low risk on one of the two conditions and high risk on the other)	5 (1.2%)
Intermediate – Intermediate (Moderate risk on both T21 and T13 / T18)	39 (9.4%)
Intermediate – High (Moderate risk on one of the two conditions and high risk on the other)	6 (1.4%)
High – High (High risk on both T21 and T13 / T18)	2 (0.5%)
	N = 414 (100%)

As seen in Table 3.4, overall there were 253 participants that were low risk on all chromosomal abnormalities tested for and all of them chose to have no further test.

The remaining 161 participants had some level of risk (moderate or high) on one or both the conditions tested for. Out of these, four chose to have an invasive test (CVS), 151 chose to have NIPT, and six decided to have no further testing at all. This is in line with recent evidence whereby, when women were offered the additional option of NIPT over invasive tests, the majority of high risk and 90% of intermediate risk women chose to have a NIPT (Gil et al, 2014). With studies including NIPT in women's options only recently emerging there are no official national statistics to draw upon, but a 26% drop in uptake of invasive tests and a 95% decrease in women who would have chosen no further testing prior to the introduction of NIPT, have been reported (Gil et al, 2014).

3.3.2. Sample description

The vast majority of the sample (n=290, 69%) was white and of a European, Middle Eastern, North African or Hispanic ethnic origin. A further 77 participants (18%) were black African, Caribbean, or African American. The remaining sample comprised of East Asian (n=20, 2%), South Asian (n=25, 6%), and mixed (n=15, 4%) ethnic origins. The mean age was 35.4, with ages ranging from 19 to 45. The majority of women (n=258, 61.3%) had a university postgraduate degree, while a further 84 (19.9%) reported having either a university or a college degree, and 69 (16.4%) had graduated from secondary school.

In terms of religion, almost half the sample (n=201, 48%) was Christian, and nearly as many participants (n=174, 42%) reported having no religion. Out of the remaining participants, 32

reported being Muslims, Hindus or Buddhists whereas a further 5 stated 'other' religion and 4 refused to disclose such information.

The vast majority of women (n=358, 85.6%) were living with a partner whether married or not and 41 (9.8%) were in a relationship but not living together. Sixteen women (3.8%) reported not being in a relationship at the time of the survey and a further 3 (0.7%) declined to disclose their marital status.

A 98% of the sample reported no family history of chromosomal abnormality as opposed to seven participants who stated they had a family member with such a condition. Likewise, the majority of the sample (n=390, 93.1%) conceived naturally, while 20 women (4.8%) had IVF treatment and seven (1.75%) took fertility drugs.

In terms of having other children the sample was fairly equally split, with 238 women (56.8%) being pregnant to their first child and the remaining 179 (42.7%) reporting having one or more other children. Furthermore, 113 women (27%) reported having had a previous miscarriage as opposed to 301 (73%) who did not.

Out of the total sample only six women (1%) reported having had an invasive diagnostic test in the past. Finally, the vast majority (253 women; 61%) stated that they got pregnant 'very easily' and a further 76 (18%) found it 'quite easy'. 33 women replied 'neutral', with 27 (6%) and 26 (6%) women stating it was 'quite difficult' or 'very difficult' respectively.

3.3.3. Mental Health and decision making regarding prenatal testing

Cross-tabulation was performed in order to account for any differences in the decision making patterns of women with mental health issues. Mental health was originally measured in terms of depression (n=8), anxiety disorder (n=6), both depression and anxiety disorder (n=3), and bipolar disorder (n=1). However, due to the small numbers they were all grouped together into a mental health group category (n=18) that was compared to the remaining non-mental health group (n=396).

The two above groups were then compared in terms of their risk status and were therefore divided into two further categories: 1) low risk on both T21 and T13/T18 (mental health vs. non-mental health) and 2) moderate/high risk on T21 and/or T13/T18 (mental health vs. non-mental health). The outcome measure was women's decision outcome (invasive test, NIPT, or no test).

Table 3.5

Comparison of low risk (on both T21 and T13/T18) mental health vs. non-mental health groups

GROUPS	Sample (n)	Decision Outcome		
		Invasive Test (CVS)	Harmony	No test
Mental Health	10	0	0	10
Non-Mental Health	243	0	0	243
Total	253	0	0	253

As seen in Table 3.5, all women who were low risk, regardless of mental health status, chose to have no further test. Therefore, no further analysis was warranted for this group since no differences are observed in the decision outcome.

Table 3.6

Comparison of intermediate / high risk (on T21 and/or T13/T18) mental health vs. non-mental health groups

GROUPS	Sample (n)	Decision Outcome		
		Invasive Test (CVS)	Harmony	No test
Mental Health	8	0	8	0
Non-Mental Health	153	4	143	6
Total	161	4	151	6

Within the intermediate / high risk group all women with a mental health issue opted for NIPT, whereas the non-Mental Health group was more varied (Table 3.6). However, there were no significant differences between the two groups $\chi^2(2, N=161) = 0.558, p = .757$ and therefore no further analysis was required in relation to women's decision making patterns.

To sum up, the comparison between women with mental health issues and women without showed that we don't have sufficient evidence to prove that having a mental health disorder influences women's decision in relation to prenatal testing. Nevertheless, due to the very small number of women with mental health problems in our sample, further studies are needed to address this issue.

3.3.4. Descriptive statistics for variables examined

Table 3.7 shows the descriptive statistics of the predictor variables. It also depicts the z-transformed statistics for predictor to predictor comparison. Normality of the distribution is explored with the use of the excess skewness and kurtosis. It is observed that the predictors

anxiety, Positive Attitudes to Doctors (PAD), Positive Attitudes to Medicine (PAM), Negative Attitudes to Doctors (NAD), Negative Attitudes to Medicine (NAM), internal, chance, powerful others locus of control, attitudes to prenatal testing, attitudes to genetic abnormality, and perceived behavioural control (PBC), have a highly-skewed distribution ($|excess| > 2$). Attempted transformations to normalise the distribution failed hence non-parametric tests will be deployed for comparisons across groups.

It is important to note that whilst we would normally adjust the level of significance so as to account for the multiple comparisons, it was decided that a significance level of $p = .05$ would be retained. The reason for this is that due to the low sample size in the high-risk group and the group that underwent invasive tests (because of the nature of the topic) this, in itself, makes it difficult to detect any statistical significance and even though adjusting the level of significance would reduce the chance of a Type I error (reporting something as significant when it really is not) it would, on the other hand, increase the chance of a Type II error (significant findings going undetected) which is not less important (Perneger, 1998; Rothman, 1990; Cole, 1979). The main purpose of this study was to add to the literature referring to prenatal testing but with the recent addition of NIPT and thus potentially prove useful for future studies (i.e. meta-analyses) that would emphasise the effect sizes reported. Therefore, a p value of .05 was considered appropriate for these purposes.

Table 3.7

Descriptive statistics for 11 variables examined prior to comparing between groups

	Anxiety Score (HADS)	Positive attitudes to doctors	Positive attitudes to medicine	Negative attitudes to doctors	Negative attitudes to medicine	Internal locus of control	Chance locus of control	Powerful Others locus of control	Attitudes to prenatal diagnostic tests	Attitudes to genetic abnormalities	Perceived behavioural control
N	419	414	414	414	414	409	408	409	410	410	410
Mean	5,365	12,604	13,464	12,580	12,324	24,538	16,934	17,929	12,471	5,693	12,032
SD	3,282	2,720	2,295	2,749	2,803	4,200	4,814	5,378	2,452	1,605	2,010
Minimum	0	5	5	6	5	9	6	6	3	2	4
Maximum	15	20	19	21	24	34	32	34	15	10	15
Range	15	15	14	15	19	25	26	28	12	8	11
Z values											
Minimum	-1,63	-2,8	-3,69	-2,39	-2,61	-3,7	-2,27	-2,22	-3,86	-2,3	-4
Maximum	2,94	2,72	2,41	3,06	4,17	2,25	3,13	2,99	1,03	2,68	1,48
Range	4,57	5,52	6,1	5,46	6,78	5,95	5,4	5,21	4,89	4,99	5,47
Reliability statistics											
Cronbach's alpha	0,757	0,723	0,466	0,573	0,615	0,638	0,621	0,717	0,7	0,436	0,768
Number of items	7	4	4	6	5	6	6	6	3	2	3
Distribution statistics											
Kurtosis	-0,072	-0,242	0,207	0,037	0,429	0,289	0,071	-0,091	0,342	-0,111	0,939
SE Kurtosis	0,238	0,239	0,239	0,239	0,239	0,241	0,241	0,241	0,24	0,24	0,24
Skewness	0,664	0,034	-0,252	0,156	0,245	-0,437	0,133	0,357	-0,865	-0,468	-0,626
SE Skewness	0,119	0,12	0,12	0,12	0,12	0,121	0,121	0,121	0,121	0,121	0,121
Excess Kurtosis	-0,30	-1,01	0,87	0,15	1,79	1,20	0,29	-0,38	1,43	-0,46	3,91
Excess Skewness	5,58	0,28	-2,10	1,30	2,04	-3,61	1,10	2,95	-7,15	-3,87	-5,17

Note: SE = Standard Error, Excess Kurtosis = Kurtosis/ SE of Kurtosis, Excess Skewness = Skewness/ SE of Skewness

a) *Low risk versus Intermediate / High Risk groups.*

Prior to any statistical analysis a description of the data is presented so as to get a first impression of the tendencies in women's decision making process. To begin with, the mean scores and standard deviations are considered for the low risk group in comparison to the intermediate / high risk group providing an overview of any different patterns between women of low risk and women who were diagnosed with some level of risk, whether moderate or high.

In general, the two groups (low risk vs. intermediate / high risk) presented with somewhat similar scores on all tested variables. Firstly, there was no significant difference in anxiety levels between women in the low risk group ($M=5.333$, $SD=3.2$) and women in the intermediate / high risk group ($M=5.429$, $SD=3.5$), $U=20131$, $p=0.89$. This is not surprising considering that questionnaires were completed before women were informed of their risk status and therefore they were all starting from a relatively same baseline.

One interesting observation was that women in the low risk group reported a more positive attitude towards doctors ($M=12.702$, $SD=2.7$) compared to women of an intermediate / high risk ($M=12.419$, $SD=2.8$) but women with some level of risk reported a more positive attitude towards medicine ($M=13.644$, $SD=2.2$) compared to women of low risk ($M=13.319$, $SD=2.4$). However, these differences between the two groups did not reach statistical significance ($t(406)=1.03$, $p=0.30$ and $U=18561$, $p=0.30$ respectively) and are therefore likely to be attributed to coincidence.

In addition, both groups reported a greater internal locus of control than 'chance' or 'powerful others', although women in the intermediate / high risk group scored relatively higher on all sources of locus of control. In accordance with the scoring instructions of the MHLOC scale (Walston, 2005) both groups had a strong inclination towards 'internal' locus of control as they scored above 23, and a moderate inclination towards 'chance' and 'powerful others' locus of control where they scored between 15 and 22 which are the cut-off points. In comparing the two groups, there was a significant difference in the 'internal locus of control' scale with women in the intermediate / high risk group ($M=25.127$, $SD=4.2$) scoring higher than women in the low risk group ($M=24.176$, $SD=4.2$), $U=216972$, $p=0.04$. In terms of the other two scales there was no significant difference, with $t(401)=-0.70$, $p=0.49$ for 'chance' locus of control, and $U=19232$, $p=0.91$ for 'powerful others' locus of control.

Women with some level of risk reported a statistically significant more positive attitude towards prenatal diagnostic tests ($M=12.791$, $SD=2.4$) compared to women of low risk ($M=12.252$, $SD=2.5$), $U=17018$, $p=0.03$. This is interesting considering that data was collected before women found out their risk level and therefore this could not have been influenced by their awareness of being at risk. Upon further exploration of the data, one potential explanation for this is that women in the intermediate / high risk group were significantly older ($M=35.54$, $SD=4.8$) than women in the low risk group ($M=30.55$, $SD=5.3$), $t(412)=-9.61$, $p<0.001$. It is possible that older women are aware of their age-related risk and thus may have developed a

more positive attitude as a protective mechanism in the event that their increased risk is confirmed and they are faced with a decision to have further testing. They may also have had more interaction with other women's positive experiences of prenatal diagnostic tests although this is difficult to assume without having specific data to back it up. On the contrary, women of low risk reported a more positive attitude towards genetic abnormalities ($M=5.764$, $SD=1.6$) than women of intermediate / high risk ($M=5.589$, $SD=1.6$) although the difference did not reach statistical significance, $U=18190$, $p=0.27$. This again may be explained by the significant difference in age between the two groups: younger women may believe they are at a lower risk because of their age and therefore the concept of a child with a genetic abnormality may be far from them so as not to cause negative feelings and preconceptions.

Finally, women in the intermediate / high risk group reported a slightly higher level of perceived behavioural control ($M=12.139$, $SD=2.0$) than women in the low risk group ($M=11.935$, $SD=2.0$). This is quite important as these women were subsequently faced with the decision to take up further diagnostic testing or not and thus having a sense of control is something that is likely to have aided this process. However, it is important to note that the difference between the two groups was not statistically significant, $U=18328$, $p=0.33$.

Table 3.8

Means (M) and Standard Deviations (SD) for questionnaire variables, for low and moderate/high risk groups respectively

		Anxiety Score (HADS)	Positive attitudes to doctors	Positive attitudes to medicine	Negative attitudes to doctors	Negative attitudes to medicine	Internal locus of control	Chance locus of control	Powerful Others locus of control	Attitudes to prenatal diagnostic tests	Attitudes to genetic abnormalities	Perceived behavioural control
Low Risk	N	252	248	248	248	248	245	244	245	246	246	246
Raw scores	Mean	5.333	12.702	13.319	12.520	12.557	24.176	16.770	17.886	12.252	5.764	11.935
	SD	3.2	2.7	2.4	2.7	2.8	4.2	4.7	5.4	2.5	1.6	2.0
Z value scores	Mean	-0,0087	0,0359	-0,0633	-0,0217	0,083	-0,0863	-0,0339	-0,0081	-0,0892	0,0446	-0,0481
	Min	-1,63	-2,8	-3,69	-2,39	-2,61	-3,7	-2,27	-2,22	-3,86	-2,3	-4
	Max	2,94	2,72	2,41	3,06	4,17	2,25	2,71	2,99	1,03	2,06	1,48
	Range	4,57	5,52	6,1	5,46	6,78	5,95	4,99	5,21	4,89	4,36	5,47
Moderate / High Risk	N	161	160	160	160	160	158	158	158	158	158	158
Raw scores	Mean	5.429	12.419	13.644	12.675	12.019	25.127	17.114	18.006	12.791	5.589	12.139
	SD	3.5	2.8	2.2	2.8	2.8	4.2	5.0	5.4	2.4	1.6	2.0
Z value scores	Mean	0,0026	-0,0049	-0,0077	0,0004	0,0078	0,0025	-0,0059	0,0007	-0,0032	0,0018	-0,0084
	Min	-1,63	-2,8	-3,69	-2,39	-2,61	-3,7	-2,27	-2,22	-3,86	-2,3	-4
	Max	2,94	2,72	2,41	3,06	4,17	2,25	3,13	2,99	1,03	2,68	1,48
	Range	4,57	5,52	6,1	5,46	6,78	5,95	5,4	5,21	4,89	4,99	5,47
T tests/ Mann Whitney U	T/ U	20131	1.03	18561	-0.55	17174	216972	-0.70	19232	17018	18190	18328
Level of significance	P	0.89	0.30	0.30	0.58	0.02*	0.04*	0.49	0.91	0.03*	0.27	0.33

Note. * indicates statistical significance at the 0.05 level, t-test for Positive attitudes to doctors, Negative attitudes to doctors, Chance locus of control. Mann-Whitney U test for the rest of the variables

b) Intermediate / High risk group: comparison within groups based on decision outcome

Further insight to the intermediate / high risk group in terms of their decision outcome (invasive test vs. NIPT vs. no testing) was considered plausible in order to identify any indications of potential different patterns in the decision-making process.

As observed in Table 3.8, there was no significant difference amongst the three groups on any of the factors under examination. However, extremely unequal sample sizes may affect the homogeneity of variances assumption and bias the statistical significance (Field, 2013; p175). Therefore effect sizes were also calculated to provide further insight to any differences between the no-test group and each of the other two groups (CVS and NIPT groups respectively)

Table 3.9

Means (M) and Standard Deviations (SD) for questionnaire variables in relation to decision outcome within the moderate / high risk group

		Anxiety Score (HADS)	Positive attitudes to doctors	Positive attitudes to medicine	Negative attitudes to doctors	Negative attitudes to medicine	Internal locus of control	Chance locus of control	Powerful Others locus of control	Attitudes to prenatal diagnostic tests	Attitudes to genetic abnormalities	Perceived behaviour al control
CVS	N	4	4	4	4	4	4	4	4	4	4	4
Raw Scores	Mean	3.75	14.75	15.75	12.75	13.25	27.25	14.25	17.25	14.75	4.5	12.25
	SD	1.5	1.3	1.5	1.0	4.3	1.7	3.4	4.1	0.5	1.3	0.5
Z value scores	Mean	-0,491	0,789	0,996	0,062	0,331	0,6458	-0,558	-0,126	0,930	-0,743	0,109
	Minimum	-0,72	0,15	0,23	-0,21	-1,19	0,11	-1,23	-1,1	0,62	-1,68	-0,02
	Maximum	0,19	1,25	1,54	0,52	2,38	1,06	0,43	0,76	1,03	0,19	0,48
	Range	0,91	1,1	1,31	0,73	3,57	0,95	1,66	1,86	0,41	1,87	0,5
Harmony	N	151	150	150	150	150	148	148	148	148	148	148
Raw scores	Mean	5.4437	12.387	13.633	12.653	11.947	25.142	17.068	17.919	12.764	5.635	12.169
	SD	3.6	2.7	2.2	2.9	2.7	4.2	5.0	5.4	2.4	1.6	2.0
Z value scores	Mean	0,0249	-0,0799	0,0739	0,0268	-0,1345	0,1438	0,0278	-0,0019	0,1194	-0,0359	0,0683
	Minimum	-1,63	-2,43	-1,95	-2,39	-2,61	-2,75	-2,27	-1,85	-3,86	-2,3	-4
	Maximum	2,94	2,35	2,41	3,06	2,38	2,01	3,13	2,62	1,03	2,68	1,48
	Range	4,57	4,78	4,36	5,46	4,99	4,76	5,4	4,46	4,89	4,99	5,47
No test	N	6	6	6	6	6	6	6	6	6	6	6
Raw score	Mean	6.1667	11.667	12.5	13.167	13	23.333	20.167	20.667	12.167	5.167	11.333
	SD	3.9	3.6	2.2	2.6	3.2	4.9	4.7	5.4	2.7	1.0	2.2
Z value scores	Mean	0,2452	-0,3446	-0,42	0,2135	0,2413	-0,2868	0,6716	0,5091	-0,124	-0,3278	-0,3474
	Minimum	-1,02	-2,06	-1,51	-0,57	-0,83	-2,27	-0,61	-0,54	-2,23	-1,05	-2,01
	Maximum	2,33	1,25	0,67	1,97	1,67	1,06	1,68	2,06	0,62	0,19	0,98
	Range	3,35	3,31	2,18	2,55	2,5	3,33	2,29	2,6	2,86	1,25	2,98

		Anxiety Score (HADS)	Positive attitudes to doctors	Positive attitudes to medicine	Negative attitudes to doctors	Negative attitudes to medicine	Internal locus of control	Chance locus of control	Powerful Others locus of control	Attitudes to prenatal diagnostic tests	Attitudes to genetic abnormalities	Perceived behaviour al control
Level of significance	p ¹	0,752	0,238	0,174	0,885	0,366	0,239	0,184	0,459	0,194	0,383	0,599
No test vs. CVS	Cohen's d ²	0,76	1,04	1,67	0,19	0,07	0,97	1,39	0,69	1,19	0,60	0,76
No test vs. Harmony	Cohen's d	0,20	0,26	0,52	0,18	0,39	0,43	0,63	0,51	0,25	0,30	0,20

Note. ¹ Kruskal-Wallis

² Cohen's d effect sizes: 0.20=small effect size, 0.50=medium effect size, and 0.80=large effect size.

c) *Effect sizes for no test group vs. Amniocentesis / CVS group*

Interestingly the effect sizes were mostly large on the majority of variables between women who chose to have no further testing and women who chose to have a CVS (Table 3.9). This suggests that with a larger sample size it is most likely that there would be a significant difference between these two groups on these factors (anxiety levels; positive attitudes to doctors; positive attitudes to medicine; internal locus of control; chance locus of control; powerful others locus of control; attitudes to prenatal diagnostic testing; and, perceived behavioural control).

Based on the 'large' effect sizes it appears that women who chose to have a CVS, have more positive attitudes to doctors ($M=14.75$, $SD=1.3$) and medicine ($M=15.75$, $SD=1.75$) compared to women who chose to have no further test ($M=11.667$, $SD=3.6$ and $M=12.5$, $SD=2.2$ respectively). In addition, women in the CVS group reported a greater internal locus of control ($M=27.25$, $SD=1.7$) than women in the 'no test' group ($M=23.333$, $SD=4.9$), whereas women who chose to have no further testing reported a greater 'chance' locus of control ($M=20.167$, $SD=4.7$) than women who opted for a CVS ($M=14.25$, $SD=3.4$). In addition, women in the CVS group reported a more positive attitude towards prenatal diagnostic tests ($M=14.75$, $SD=0.5$) than women in the 'no test' group ($M=12.167$, $SD=2.7$), and a greater perceived behavioural control ($M=12.25$, $SD=0.5$ vs. $M=11.333$, $SD=2.2$). One interesting finding is that women who chose to have no test reported greater levels of anxiety ($M=6.1667$, $SD=3.9$) than women who chose to have a CVS ($M=3.75$, $SD=1.5$).

d) *Effect sizes for no test group vs. NIPT group.*

In terms of comparing women who chose to have no further testing to women who opted for NIPT, no large effect sizes were identified. However, there were several 'medium' effect sizes, indicating that the relative magnitude of differences between the two groups "*would be large enough to be visible to the naked eye*" (Cohen, 1988, p.26) should the comparable samples be of a more equal size. More specifically, these results suggest that women in the NIPT group have more positive attitudes to medicine ($M=13.633$, $SD=2.2$) than women in the 'no test' group ($M=12.5$, $SD=2.2$). Likewise, women who chose to have a Harmony test reported a greater 'internal' locus of control ($M=25.142$, $SD=4.2$) than women who chose no further testing ($M=23.333$, $SD=4.9$). On the contrary, women in the 'no test' group had a greater 'chance' locus of control ($M=20.167$, $SD=4.7$) than women in the NIPT group ($M=17.068$, $SD=5.0$) as well as a greater 'powerful others' locus of control ($M=20.667$, $SD=5.4$ vs. $M=17.25$, $SD=4.1$).

3.3.5. Logistic Regression

Logistic regression Analyses were subsequently carried out in order to assess the cumulative effect of the variables under investigation to the decision to have an invasive, a non-invasive or

no further test at all. Logistic regression, as a multivariate analysis, will adjust the effect of all the factors under consideration and surface the statistically significant factors towards decision making.

a) The role of the psychological factors under investigation in women's decision to have an invasive test (CVS)

Initially, logistic regression was carried out on the overall sample (N=414) to explore the role of the 11 variables under investigation on the decision to have an invasive test (CVS).

As illustrated in Table 3.10, none of the 11 variables under investigation were shown to have a significant impact, with a 0.05 level, on women's decision to have an invasive test. However, a tendency is observed in three of the variables and their impact on women's decision to have a CVS test. More specifically, anxiety levels were negatively associated with the decision outcome (odds ratio=0.60, $p=0.08$) suggesting that a woman with increased levels of anxiety is less likely to choose to have an invasive test. In addition, negative attitude to medicine (NAM) and attitudes to prenatal testing (Apretest) were both positively associated with the decision outcome leading to a somewhat controversial finding: women with a negative attitude towards medicine are suggested to be more likely to have an invasive test (odds ratio=1.47, $p=0.07$) whilst on the other hand, women with a positive attitude to prenatal testing are also more likely to have an invasive test (odds ratio=2.43, $p=0.07$).

Table 3.10

Firth Logistic Regression on the role of psychological factors in decision to have a CVS (N=414)

	coef	se(coef)	Chisq	p	Odds ratio
(Intercept)	-35.34	11.83	8.84	0.00	0.00
Anxiety	-0.50	0.23	3.11	0.08	0.60
PAD	0.64	0.29	2.59	0.11	1.89
PAM	0.62	0.31	2.66	0.10	1.85
NAD	0.47	0.26	1.62	0.20	1.59
NAM	0.39	0.18	3.30	0.07	1.47
ILC	0.16	0.11	0.62	0.43	1.10
CLC	-0.26	0.12	2.69	0.10	0.77
POLC	-0.14	0.09	1.41	0.23	0.87
APreTest	0.89	0.43	3.31	0.07	2.43
AGenAbn	-0.12	0.32	0.10	0.75	0.89
PBC	-0.23	0.24	0.54	0.46	0.80

Note. PAD = positive attitude to doctors; PAM = positive attitude to medicine; NAD = negative attitude to doctors; NAM = negative attitude to medicine; ILC = internal locus of control; CLC = chance locus of control; POLC = powerful others locus of control; APreTes = attitude to prenatal testing; AGenAbn = attitude to genetic abnormality; PBC = perceived behavioural control

Likelihood ratio test=16.54877 on 11 df, p=0.1219494, n=414

b) The role of the psychological factors under investigation in women's decision to have NIPT

A regression analysis was also carried out on the overall sample (N=414) to explore the role of the 11 variables under investigation on the decision to have NIPT.

As illustrated in Table 3.11 three factors reached statistical significance. More specifically, women with a negative attitude to doctors (NAD) are more likely to have a non-invasive test (odds ratio=1.10, p=0.05) as are women with an internal locus of control (odds ratio=1.06, p=0.02). On the other hand, women with a negative attitude to medicine (NAM) are less likely to have a non-invasive test (odds ratio=0.88, p=0.01) as this variable was negatively associated with the decision outcome.

Table 3.11

Firth Logistic Regression on the role of psychological factors in decision to have NIPT (N=414)

	coef	se(coef)	Chisq	p	odds ratio
(Intercept)	-2.93	1.78	2.82	0.09	0.05
Anxiety	0.01	0.03	0.06	0.80	1.01
PAD	-0.08	0.05	2.66	0.10	0.93
PAM	0.07	0.05	1.85	0.17	1.08
NAD	0.09	0.05	3.64	0.05	1.10
NAM	-0.12	0.05	6.53	0.01	0.88
ILC	0.06	0.03	5.05	0.02	1.06
CLC	0.02	0.03	0.37	0.55	1.02
POLC	0.01	0.02	0.38	0.58	1.01
APreTest	0.08	0.05	2.27	0.13	1.08
AGenAbn	-0.01	0.08	0.01	0.93	0.99
PBC	-0.02	0.06	0.07	0.79	0.98

Note. PAD = positive attitude to doctors; PAM = positive attitude to medicine; NAD = negative attitude to doctors; NAM = negative attitude to medicine; ILC = internal locus of control; CLC = chance locus of control; POLC = powerful others locus of control; APreTest = attitude to prenatal testing; AGenAbn = attitude to genetic abnormality; PBC = perceived behavioural control

Likelihood ratio test=20.79106 on 11 df, $p=0.03560153$, $n=414$

c) *The inclusion of risk status as a predictive variable in the decision to have an invasive test (CVS)*

Logistic regression of CVS as the chosen test (0=otherwise) on the risk status for T21 and T13/T18, and the psychological factors (Anxiety, PAD, PAM, etc.) has shown the statistically significant effect of the T21 risk status ($p=0.04$) on the final decision of pregnant women towards CVS. The results indicate that in the presence of risk for T21, the results regarding risk for T13/T18 do not contribute to the decision of the pregnant woman towards CVS ($p=0.37$). Likewise, no psychological factors statistically contribute to the decision towards CVS (Table 3.12).

Table 3.12

Firth Logistic regression on CVS (N=414), including risk for T21 and T13/T18

	b	se(b)	Chi-square	p	Odds Ratio
(Intercept)	-7.11	7.21	0.18	0.67	0.00
T21	1.93	0.74	4.03	0.04	6.86
T13/T18	1.41	0.86	0.82	0.37	4.11
Anxiety	-0.30	0.16	1.32	0.25	0.74
PAD	0.31	0.22	0.60	0.44	1.36
PAM	0.16	0.26	0.07	0.79	1.17
NAD	0.03	0.22	0.00	1.00	1.02
NAM	0.28	0.19	1.36	0.24	1.32
ILC	-0.03	0.13	0.02	0.89	0.97
CLC	-0.29	0.12	1.15	0.28	0.74
POLC	-0.07	0.09	0.17	0.68	0.93
APreTest	-0.15	0.21	0.23	0.63	0.85
AGenAbn	-0.31	0.33	0.40	0.53	0.73
PBC	-0.09	0.21	0.08	0.78	0.91

Note. PAD = positive attitude to doctors; PAM = positive attitude to medicine; NAD = negative attitude to doctors; NAM = negative attitude to medicine; ILC = internal locus of control; CLC = chance locus of control; POLC = powerful others locus of control; APreTest = attitude to prenatal testing; AGenAbn = attitude to genetic abnormality; PBC = perceived behavioural control

Dependent variable CVS (1= CVS, 0=Otherwise). 4 cases (0.9%) with CVS as the chosen test. Likelihood ratio test=25.57, df(13), p=0.0193, AIC = 0.424. Model fitted by Penalized Maximum Likelihood Estimation (Firth Logistic).

Nonetheless, even though there is no statistically significant effect of any of the psychological factors on the decision to have an invasive test, a closer look at the odds ratio values (Table 3.12) indicates some tendencies that may be of interest to take into consideration. An odds ratio indicates the odds of an outcome occurring in the presence of a particular event happening as opposed to the odds of it happening in the absence of that event and therefore, even if not statistically significant it provides important information in that it reveals a tendency that may become significant, i.e. in the presence of a bigger sample size and even if not, the size of the OR (>1) may be indicative of factors that may still influence the outcome to some extent. For example, a more positive attitude to doctors (PAD) indicates that the likelihood of a woman having a CVS is increased (odds ratio=1.36). Likewise, but to a slightly lesser degree, a positive attitude to medicine (PAM) seems to also increase the odds of a woman choosing an invasive test (odds ratio=1.17). Interestingly, negative attitudes to medicine (NAM) seem to have a greater effect on the decision to have a CVS by increasing the likelihood of a woman making this choice (odds ratio=1.32).

d) *The inclusion of risk status as a predictive variable in the decision to have a non-invasive test (Harmony)*

We proceeded with excluding the cases (N=4) where CVS was chosen, and investigated the association of T21 and T13/T18 risk status as well as the psychological factors to the decision towards NIPT (NIPT N=151-36.8% vs. No Test N=259-63.2%). Results of the firth logistic

regression indicate the significance of both T21 results ($p < 0.0001$) and the T13/T18 results ($p < 0.0001$) in the decision to have NIPT (Likelihood=444.16 $p < 0.0001$). The psychological factors remain insignificant to the model

Table 3.13

Firth Logistic regression on NIPT (N=410) including risk for T21 and T13/T18

	b	se(b)	Chisquare	p	Odds Ratio
(Intercept)	-32.15	7.64	24.06	<0.001	1.08
T21	8.68	1.27	Inf	<0.001	0.01
T13/T18	7.33	1.45	55.42	<0.001	0.00
Anxiety	0.02	0.09	0.04	0.850	1.02
PAD	0.16	0.15	0.84	0.360	1.17
PAM	0.19	0.18	0.86	0.350	1.21
NAD	0.13	0.15	0.55	0.460	1.14
NAM	-0.08	0.15	0.22	0.640	0.92
ILC	0.07	0.08	0.63	0.430	1.07
CLC	-0.02	0.09	0.03	0.850	0.98
PLC	-0.08	0.09	0.65	0.420	0.92
APreTest	0.13	0.15	0.49	0.480	0.11
AGenAbn	0.13	0.24	0.22	0.640	1.14
PBC	0.23	0.18	1.14	0.280	1.25

Note. PAD = positive attitude to doctors; PAM = positive attitude to medicine; NAD = negative attitude to doctors; NAM = negative attitude to medicine; ILC = internal locus of control; CLC = chance locus of control; POLC = powerful others locus of control; APreTest = attitude to prenatal testing; AGenAbn = attitude to genetic abnormality; PBC = perceived behavioural control

Nonetheless, despite not reaching statistical significance a closer look at the odds ratio values (Table 3.13) indicates that a more positive attitude towards medicine (PAM) increases a woman's likelihood to have NIPT (odds ratio=1.21), as does an increased perceived behavioural control (PBD) (odds ratio=1.25).

e) The impact of the psychological factors under investigation on the decision to have NIPT in women who were low risk in T13/T18 but intermediate risk for T21

Further analysis was carried out in order to cross-tabulate patients' test decision by the T13/T18 and T21 risk status results (Table 3.14). At a LOW risk for T13/T18, we observe that 99 out of 357 (27.7%) patients chose to do NIPT over 'No test at all', while only 9 out of 263 (3.4%) patients at LOW risk for T21 chose to do NIPT (Table 3.14). This is probably due to the fact that 95 out of the 99 LOW T13/T18 patients also had an intermediate risk for T21. This indicates the significance of an identified risk for T21 (over the T13/T18 risk) towards the decision to have NIPT.

Table 3.14

Patients' decision outcome depending on risk for T13/T18

Participant's risk status for T13 or T18	Participant's risk status for T21	Which test did the patient decide to have?			
		Amnio / CVS	Harmony	No test	Total
Low (<1:2500)	Low (<1:2500)	0	0	253	253
	Intermediate (>1:2500)	0	95	5	100
	High (>1:100)	0	4	0	4
	Total	0	99	258	357
Intermediate (>1:2500)	Low (<1:2500)	0	8	1	9
	Intermediate (>1:2500)	0	39	0	39
	High (>1:100)	4	2	0	6
	Total	4	49	1	54
High (>1:100)	Low (<1:2500)	0	1	0	1
	High (>1:100)	0	2	0	2
	Total	0	3	0	3
GRAND TOTAL		4	151	259	414

Due to the above finding (Table 3.14) that the vast majority of women who were considered low risk for T13/T18 but moderate risk for T21 (N=100) chose to have NIPT (N=95) a logistic regression was also carried out in order to account for the contribution of the factors under investigation in this decision and identify any different patterns with the previous groups.

Table 3.15

Patients' decision outcome depending on risk for T21

Participant's risk status for T21	Participant's risk status for T13 or T18	Which test did the patient decide to have?			
		Amnio / CVS	Harmony	No test	Total
Low (<1:2500)	Low (<1:2500)	0	0	253	253
	Intermediate (>1:2500)	0	8	1	9
	High (>1:100)	0	1	0	1
	Total	0	9	254	263
Intermediate (>1:2500)	Low (<1:2500)	0	95	5	100
	Intermediate (>1:2500)	0	39	0	39
	Total	0	134	5	139
High (>1:100)	Low (<1:2500)	0	4	0	4
	Intermediate (>1:2500)	4	2	0	6
	High (>1:100)	0	2	0	2
	Total	4	8	0	12
GRAND TOTAL		4	151	259	414

None of the variables under investigation reached statistical significance for this group of women. However, a closer look at the odds ratio values indicates some tendencies that may be

of interest for future research. Firstly, it is suggested that a positive attitude to doctors (PAD) as well as a positive attitude to medicine (PAM) increase the likelihood of a woman in this category (low risk for T13/T18 and moderate risk for T21) to have NIPT (odds ratio=1.27 and 1.29 respectively). Likewise, a positive attitude to prenatal testing and a positive attitude to genetic abnormalities also increase the likelihood of a Harmony test in this group (odds ratio=1.21 and 1.29 respectively). Finally, to an even greater extent than the aforementioned, an increased perceived behavioural control (PBC) also increases the likelihood of a woman in this group to have NIPT (odds ratio=1.37).

Table 3.16

Logistic regression of NIPT test decision for LowT13/T18 and Moderate T21 risk (N=100)

	Zelig Logistic			Firth Logistic		
	B	p	Odds Ratio	b	p	Odds Ratio
(Intercept)	-11.20	0.31	<0.0001	-12.75	0.1	2.91
Anxiety	0.03	0.87	1.02	0.02	0.9	1.02
PAD	0.20	0.43	1.22	0.24	0.20	1.27
PAM	0.19	0.49	1.21	0.26	0.23	1.29
NAD	0.16	0.52	1.17	0.10	0.62	1.11
NAM	-0.03	0.92	0.97	0.03	0.88	1.03
ILC	0.07	0.54	1.07	0.08	0.42	1.08
CLC	-0.004	0.98	0.99	-0.01	0.93	0.99
POLC	-0.09	0.54	0.91	-0.11	0.38	0.90
APreTest	0.18	0.43	1.19	0.19	0.32	1.21
AGenAbn	0.15	0.70	1.17	0.26	0.44	1.29
PBC	0.29	0.33	1.33	0.31	0.17	1.37
AIC = 51.822			AIC=13.63			

Note. AIC=An Information Criterion, used for comparing the goodness of fit between the two models.

f) The role of socio-demographic factors in women's decision making process

Due to the limited number of participants choosing to have an invasive test (CVS; N=4), the role of socio-demographic factors was only explored in relation to women's decision to have a non-invasive test (NIPT; N=151). As illustrated in Table 3.17, in the presence of risk for T21 and/or T13/T18 there is no significant effect of any of the socio-demographic factors on women's decision to have NIPT. In other words, when a woman has some element of risk identified neither the psychological factors under investigation nor the socio-demographic characteristics affect her decision making process but rather, it is only her risk status that significantly affects her decision to have NIPT.

Table 3.17

The role of psychological factors, risk status and socio-demographics in women's decision making process

	coef	se(coef)	ChiSq	p	Odds ratio
(Intercept)	-29.83	7.09	21.26	<0.001	0.00
t21	8.43	1.19	Inf	<0.001	4595.33
t1318	7.04	1.36	54.01	<0.001	1140.05
black	-1.09	1.17	0.73	0.393	0.34
white	0.96	1.03	0.56	0.456	2.62
religious	0.82	0.81	0.67	0.414	2.28
degree	-0.62	1.01	0.24	0.625	0.54
post	0.63	1.44	0.08	0.784	1.87
anxiety	0.01	0.10	0.01	0.942	1.01
PAD	0.14	0.16	0.44	0.506	1.15
PAM	0.14	0.18	0.42	0.516	1.16
NAD	0.07	0.14	0.17	0.682	1.07
NAM	-0.06	0.15	0.12	0.734	0.94
ILC	0.09	0.078	0.92	0.338	1.09
CLC	0.04	0.09	0.10	0.746	1.04
POLC	-0.08	0.08	0.54	0.463	0.92
APreTest	0.07	0.13	0.19	0.663	1.07
AGenAbn	-0.06	0.22	0.05	0.829	0.94
PBC	0.21	0.19	0.57	0.449	1.23

Likelihood ratio test=434.5616 on 18 df, p<0.001, n=392

3.4. Discussion

The aim of this study was to explore women's decision making process in relation to uptake of prenatal diagnostic tests including NIPT. Using a questionnaire that was previously validated through a pilot study, the following factors were explored: anxiety levels; attitudes to doctors and medicine; attitudes to prenatal testing; attitudes to genetic abnormalities; locus of control; and, perceived behavioural control.

Initially, the role of the aforementioned factors was explored in relation to the decision to have an invasive or non-invasive test separately. Firstly, women with a more negative attitude towards medicine were found to be more likely to have an invasive test (CVS) (although results did not reach statistical significance, a clear tendency was observed) and less likely to have a non-invasive test (NIPT). While at a first glance, this finding appears controversial it is

interesting to explore potential explanations for this. For instance, unsurprisingly a woman who is not particularly invested in medicine is more likely to be critical of new interventions and thus less trusting towards newly developed tests such as NIPT. However, despite a sceptical approach towards medicine in general she may still be positively inclined towards well established screening / diagnostic tests such as CVS and amniocentesis that have proven efficiency throughout several years.

In addition, there may be a contextual effect that could shed light on this finding, as previously suggested in the literature. Conroy et al (2002), reported a striking difference in women's attitudes depending on context, with participants reporting a more negative view of the medical profession in general than their family medical practice and even more so their antenatal care service, suggesting that a more intense interaction with a medical service is associated with a more positive attitude. Within this context, an alternative explanation for the seemingly controversial results could be that the questionnaire used in this study measured attitudes to medicine in general thus potentially masking the real attitudes that are relevant within a more specific antenatal care service context. This could also account for another finding of this study whereby, a negative attitude to doctors significantly predicted uptake of NIPT. In their study, Conroy et al (2002) reported 40% of participants viewing all doctors as good doctors, compared to 85% viewing their family doctors as good doctors and almost 100% expressing a belief that the doctor looking after their pregnancy was a good doctor. Therefore, it is possible that the results of this study could be different if a measure tailored to explore more specifically women's attitudes towards their antenatal care doctors rather than doctors in general had been used.

As expected, and even though this was not statistically significant, a more positive attitude to prenatal testing would appear to predict uptake of invasive diagnostic tests such as CVS. This contradicts the findings of a qualitative study by Garcia et al (2002) where both acceptors and decliners of prenatal testing expressed positive attitudes towards the offering of prenatal testing and therefore could not be accounted for as a predictor of their decision outcome. However, within that study women who declined invasive testing called upon ethical principles and parents' obligation not to take risks on their baby's health therefore drawing upon invasive tests' negative attributes and thus indirectly expressing a negative view that may have affected their decision to one degree or another.

Shedding some light on these discrepant findings an earlier study that used a combination of questionnaire and interview methods found that even though in the close-ended questionnaire most women expressed positive attitudes towards prenatal testing when given the opportunity to elaborate through an interview they also showed awareness of and some concern over the negative aspects of such procedures (Moyer et al, 1999). Therefore, it is possible that the methodology (questionnaire-based) of our study only captured part of women's attitudes and a less structured approach may have revealed a more balanced view leading to potentially different results.

Alternatively, it could be argued that attitudes could be categorized into those focusing on a specific target (i.e. CVS) and those focusing on behaviours that are directed towards specific targets (i.e. having a CVS) (Bryant et al, 2010). Whilst one may generally value the offering of a diagnostic test, she may call upon other, such as ethical and moral, values in shaping her attitude towards taking up the test herself. The scale used in our study measured attitudes towards prenatal tests and therefore it would be interesting to explore this in relation to more explicitly measuring attitudes towards one having a diagnostic test.

In terms of invasive diagnostic test (CVS) uptake, no significant findings were reported, yet a tendency was observed in the role of anxiety and the decision outcome, which is of interest to consider. Interestingly, it was revealed that the higher the anxiety levels the less likely the woman was to choose to have a CVS. While there is evidence in the literature describing fluctuations in women's emotional state throughout pregnancy and particularly during the decision making process for prenatal diagnosis (Kaiser et al, 2004) most studies have focused on measuring anxiety levels in women who have already been identified as being at a greater risk either due to increased maternal age or first trimester screening procedures (Heyman et al, 2006). Within this group of women, elevated levels of anxiety –triggered by doubts and fear regarding foetal integrity (Hertling-Schaal, Perrotin, De Poncheville, Lansac, & Body -Schaal, 2001) - have been reported, and these are followed by a drop in most cases after receiving reassuring results (Kaiser et al, 2004). In addition, and contrary to our findings, other research has shown that for women with an identified higher risk profile, anxiety is reportedly a major reason for which they choose to have an invasive diagnostic procedure with some even reporting it to be the only reason for this decision as a means to seek reassurance (Cederholm & Sjoden, 1999). Nonetheless, due to our study being prospective and therefore data being collected prior to women finding out their risk status it is difficult to make any direct comparisons with such previous studies. It is still important, however, to consider wider evidence as well as potential explanations for our findings.

Taking a closer look at other evidence, a study by Marteau et al (1989) found no difference in anxiety levels between women who chose to have an invasive test and women who declined it during the first trimester suggesting that they all start from similar levels and anxiety is not a decisive factor during this process. This again contradicts our findings according to which there is a tendency in women who decline invasive testing to have markedly higher levels of anxiety.

In terms of the present findings, the observed difference in anxiety levels between those who chose and those who declined further testing may be reflecting a difference in coping styles with the importance of this previously having been stressed in the literature in relation to women's experience of threat of giving birth to a child with a chromosomal abnormality or other congenital defect (Bodegird, Fyro, & Larsson, 1988). A possible explanation is that our participants, having just had their first trimester scan but not received their results yet may have become more aware of the potential adverse outcome ahead therefore becoming more anxious but dealing with any such concerns over their baby's health by avoiding them and thus choosing not to have any further testing. Based on the study by Marteau et al (1989), however,

it appears that untested women's anxiety tends to increase throughout pregnancy as compared to women who do proceed with invasive diagnosis. Therefore, it would have been interesting to have had a follow-up measure and explore whether this indeed is the case for our sample as well. In that case this would highlight a potentially vulnerable group of women and would call for the development of appropriate support tools and resources that would enable a smoother journey for both the mother and the unborn baby. Alternatively, another explanation may be that the increased anxiety in women who chose to forego invasive diagnostic testing was due to other secondary factors that coincided with the timing of the testing but was not caused by this. Use of a more specific measure, tailored to pregnancy factors, may be able to shed more light on this suggestion. Nonetheless, while the above considerations may be of research and clinical research it is important to bear in mind that only a tendency was observed rather than a statistically significant finding and therefore further research would be required before drawing firm conclusions.

A final factor that was found to significantly predict uptake of non-invasive prenatal testing (NIPT) whilst risk status was controlled for, was internal health locus of control. This is not surprising, as it has been suggested that an internal locus of control is associated with positive health behaviours (Turrieff-Jonasson, 2004) as well as health-related information seeking (Wallston, Maides, & Wallston, 1976), whereas a 'chance' or 'powerful others' locus of control has been associated with a sense of powerlessness and the adoption of more unhealthy lifestyles (Steptoe & Wardle, 2001). Therefore, pregnant women in our sample with an internal locus of control may have viewed prenatal testing as part of prenatal care and therefore a health promoting behaviour that they were willing to engage in in their attempt to exert positive control over their foetus's health. This is in line with previous studies that have also found that an internal health locus of control predicted women's inclination to undergo screening and invasive testing (Lumley et al, 2006) and in comparison to couples who did not undergo screening, those who did were found to perceive a greater responsibility for their own actions and how these would impact on their unborn baby's health (Henneman et al, 2001). However, whilst previous studies have confirmed the predictive value of locus of control in relation to prenatal genetic testing attitudes, others have led to some counter-intuitive findings whereby a chance locus of control instead of an internal locus of control was positively correlated with willingness to undergo prenatal testing (Furr and Seger, 1998).

Such mixed results together with the fact that in our study internal locus of control was only found to have a predictive value in relation to non-invasive testing (NIPT) but not invasive procedures (CVS), lend themselves to further exploration in future studies. This is especially due to inconsistencies with other studies where it has been reported that internal locus of control – defined as one's belief in their own ability to control their health – is associated with the decision making process regarding genetic testing (Chen & Goodson, 2007). It may be that a more specific measure to pregnancy behaviours would be more appropriate when exploring locus of control in relation to prenatal testing. While the Multi-dimensional Health Locus of Control that was used in our study explores one's expectancies over their own health, when it comes to pregnancy the expectations tested involve women's expectations regarding the

foetus's health. Therefore, future studies could use a more tailored measure that has been developed for these purposes, namely Fetal Health Locus of Control Scale (FHLC; Labs & Wurtele, 1986). Similar to the more general scales, the FHLC also measures internal (FHLC-I), external-chance (FHLC-C), and external-powerful others (FHLC-P) dimensions with items adapted to capture subtleties related to pregnancy behaviours. Generally, FHLC-I has been found to be positively associated with positive health behaviours, such as breastfeeding (Haslam, Lawrence, & Haefeli, 2003) and information seeking on pregnancy (Sheih, Broome, & Stump, 2010), and negatively associated with negative health behaviours, such as smoking (Haslam & Lawrence, 2004), and drinking (Rao, 1997). However, only one study has used the FHLC scale in relation to prenatal testing and contrary to their original hypotheses found no significant relationships between FHLC and prenatal testing (Turrieff-Jonasson, 2004). More specifically, there were no significant differences between women who underwent maternal serum screening or amniocentesis and women who did not, on any of the three scales (internal; chance; powerful others). Therefore, whilst this measure may be valuable in determining women's health behaviours depending on their perceived control over their baby's health more research needs to be done before drawing conclusions about the reliability of the FHLC and indeed the role of locus of control in the decision-making process related to prenatal testing.

At a second stage, we added women's risk status for T21 and T13/T18 separately in the analysis so as to see whether this affects the results in any way. For both, invasive (CVS) and non-invasive (NIPT) tests, all psychological factors became insignificant and only risk was found to be significantly associated with women's decision outcome. More specifically, a greater risk for T21 was significantly associated with women's decision to have an invasive test (CVS) whereas a greater risk for either T21 or T13/T18 significantly predicted women's decision to have a non-invasive test (NIPT). Overall, these findings are in line with a previous prospective interview study where half the women participating expressed a positive attitude to undergoing invasive testing after, however, receiving their screening results, highlighting the importance of individualised risk status in this decision (Brajenovic-Milic et al, 2008). In addition, an audit report that retrospectively looked at the records of 110,180 women across four hospitals, explored the relationship between risk status following maternal serum screening (MSS) results and uptake of invasive diagnostic tests (Alberman, 2003). This audit found that risk status based on MSS results significantly predicted uptake of diagnostic tests, a finding that was also confirmed by Mueller (2005) who reported that MSS results significantly influenced women's choice of amniocentesis. Likewise, Lumley et al (2006) found that traditional risk status as determined by maternal age and family history of genetic disorders also predicted uptake of invasive testing regardless of maternal serum screening results. However, it has also been suggested that it is more the perceived risk of a woman rather than her actual risk that predicts uptake (Marteau et al, 1991) and therefore it may be of use to separate between the two before considering the impact of risk on women's participation in prenatal testing.

In terms of our findings, however, it is interesting that only an increased risk for T21 was predictive of invasive testing whereas both a greater risk for T21 and for T13/T18 were predictive of women's decision to have a non-invasive test. This means that after being

informed of their higher risk status for carrying a baby with Down's syndrome women were equally likely to either have an invasive or a non-invasive test. This in itself is not surprising as it has been previously reported that some women may want to have a definitive diagnosis and thus opt for an invasive test, whereas others –who may have previously declined any further testing due to fear of risk of miscarriage- may opt for the alternative non-invasive procedure that offers valuable information without any risks and a 99% detection rate for T21 (Chetty, 2013). In both cases, it seems that women are highly invested in getting as close to a definitive diagnosis as they can that will then aid them in subsequent decisions such as whether to terminate the pregnancy if a positive diagnosis is made or prepare for the birth and the upbringing of a baby with Down's syndrome (Fransen, 2009).

However, when women were informed of their greater risk for carrying a baby with T13 or T18 this significantly affected their decision to undergo a non-invasive test whereas it didn't seem to lead to invasive test uptake. Considering that T21 (Down's syndrome), even though non-curable, is not a lethal condition and is associated with a life expectancy of 50 years whereas most cases of T13 and T18 either die before birth or barely survive further than a few months after being born (Verweij et al, 2014), it could be assumed that women would be more inclined to find out for sure whether their baby has a life limiting condition (T13/T18) and at the same time more reluctant to take the risk of procedure related miscarriage for a foetus that may still live a relatively fulfilling life (T21). However, these results may be suggesting that regardless of the prognosis and life expectancy, women are very protective of their unborn babies and try to minimize any risks by avoiding invasive testing. In addition, the fact that only a higher risk for Down's syndrome significantly affected women's choice of invasive testing may be due to the anticipated implications of raising a child that will have some level of mental retardation, as well as an increased risk for morbidity, including leukaemia, cardiac problems and early-onset dementia (Norwitz & Levy, 2013), therefore having a potentially greater impact on them and their family unit. Nonetheless, with the non-invasive test only recently being introduced further studies of a qualitative nature would be of interest in order to explore women's choices even further.

To sum up, it appears that when risk is controlled for there are some psychological factors that affect women's decision making process regarding uptake of prenatal testing. A low level of anxiety, a negative attitude to medicine and a positive attitude to prenatal testing were all predictors of invasive diagnostic testing. On the other hand, a negative attitude towards doctors as well as medicine and an internal health locus of control were found to significantly affect women's decision to undergo a non-invasive prenatal test (NIPT). Interestingly, however, when risk was included in the analysis all psychological factors became insignificant. Within this context uptake of invasive testing (CVS) was only significantly predicted by an increased risk for T21, whereas uptake of non-invasive testing (NIPT) was predicted by both an increased risk for T21 and T13/T18. These findings suggest that whilst the decision-making process regarding prenatal testing is complex and several factors may come into play, it is women's individualized risk following the combined screening test that mostly determines decision outcome. With non-invasive testing only recently being introduced into medical practice, further research would be

required before drawing any firm conclusions. In addition, it would be interesting for future studies to further explore why women with a greater risk for T13/T18 would opt for a Harmony but not for an invasive diagnostic test. Meanwhile, based on our findings and the significant impact of identified risk, more effort should be directed towards the communication of risk to patients so as to facilitate understanding of the results and an informed decision whilst also catering to the emotional impact that such information may have on patients.

4. Chapter Four: Implications for research and practice

This study originally set out to explore the factors that influence women's decision to have an invasive prenatal diagnostic test or not. This was guided by the rationale that invasive procedures entail a risk of miscarriage and also, whilst they provide an accurate diagnosis which is considered their greatest attribute, a positive result (confirming a chromosomal abnormality) leads to subsequent critical decisions such as deciding whether to terminate the pregnancy or not (Zlotogora, 2002). However, even for women who are fully committed to seeing the whole pregnancy through, the news that they are carrying a baby with a congenital abnormality still requires a period of adjustment as well as more practical preparations for the birth of an affected foetus as well as its upbringing, i.e. through getting in touch with relevant support groups or simply seeking further information about the needs and requirements of raising a child with disabilities. Therefore, the whole prenatal diagnosis process is a multifaceted area that can have a significant impact on women's lives and thus, it is important that appropriate attention is given to ensure an informed decision and generally facilitate a smooth process for everyone involved.

Midway the study, however, the research focus had to be slightly adapted so as to incorporate a new – non-invasive – test, NIPT, that became available within our research site and which offered a highly accurate result, although not definitive, without the risk of miscarriage (ACOG, 2012). This had an immediate impact on the prenatal diagnosis scene with the vast majority of women opting for this choice and initial figures showing a 26% drop in the uptake of invasive tests as well as a 95% decrease in women who would have previously opted for no further testing (Gil, Giunta, Macalli, Poon, & Nicolaides, 2015). However, despite the encouraging progress in medical technology and the reduced risk for procedure-related losses of unaffected foetuses, those who are identified as high risk are still required to have an invasive test to confirm the result before proceeding to further decisions, thus still maintaining these types of tests an important part of the diagnostic process (Farrell, Agatisa, Mercer, Smith, & Phillipson, 2015).

From many aspects, the addition of a new non-invasive test in the prenatal diagnostic process, is a positive development with women having more options and more importantly these including highly accurate tests that eliminate the risk of miscarriage.. However, from a Health Psychology perspective the expansion of what was already a complex process also draws attention to many other elements that may easily be overlooked therefore posing different kinds of risk to women and their emotional well-being. Therefore, this section will aim to draw on key findings from this study and adopting a critical stance will attempt to consider implications for future research and practice. Research limitations of this study will also be addressed.

4.1. What do women choose – invasive or non-invasive tests?

From this study, it appears that the vast majority of women whether intermediate or high risk will opt for NIPT as opposed to an invasive test. From an open-ended question that was included in the questionnaire it appears that the elimination of risk is what makes NIPT so appealing to

women. This is something that has been reported in the literature (Farrell et al, 2015), with safety representing the key reason for women choosing NIPT especially amongst those at high risk (Lewis, Hill, & Chitty, 2016), and indicates a massive change in the prenatal diagnosis field as it leads to a significant reduction in the uptake of invasive diagnostic tests.

On the other hand, there were still women from the high-risk group that opted for the invasive test. Again, through the open-ended question that was included in the questionnaire it was apparent that the main reason for this was that an invasive test would provide them with a definitive diagnosis. This resembles findings reported elsewhere in the literature, with women preferring invasive tests over NIPT primarily because they did not feel sufficiently reassured by the results of the latter (Lewis et al, 2016). This highlights the fact that invasive diagnostic tests cannot – for the time being at least – be replaced by NIPT despite the risk of miscarriage. Should the accuracy of NIPT be further improved to resemble that of invasive tests then considerations of removing invasive tests from clinical practice will only be plausible.

An interesting finding from this study was that women who were at high risk for T13/T18 were more likely to choose a non-invasive test whereas women at a high risk of T21 would choose an invasive test. This seems counter-intuitive on two counts: firstly, the accuracy of non-invasive tests for T13/T18 is not as good as it is for T21; and secondly, the prognosis for a foetus with T13/T18 is very bleak with life expectancy being less than one year and that if they make it through the whole pregnancy (Lakovschek, Streubel, & Ulm, 2011), contrary to the life expectancy and quality of life of people with T21 which are constantly on the rise. The current questionnaire data suggests, however, that women are naturally protective of their unborn baby regardless of any potential threats, and thus factors such as severity of the condition being diagnosed do not necessarily affect their decision in relation to prenatal testing.

What this suggests is, that women from both moderate and high-risk groups show a preference for NIPT as it lifts off the concern of procedure-related miscarriage that accompanies invasive tests. This is in line with findings from the general literature whereby not only most women (Lewis et al, 2014) but also most men (van Schendele et al, 2015) report a positive attitude towards NIPT. Georgsson et al (2016) further supported this by reporting that even though most their participants were not aware of NIPT prior to taking part in their study, two thirds of them would actually consider having the test if they or their partner were pregnant. This sheds light on the importance of extended counselling being provided alongside the introduction of NIPT to clinical practice so as to facilitate an informed decision (Vanstone, King, de Vrijer, & Nisker, 2014).

However, as seen through this study women also greatly value the accuracy of invasive tests and therefore this would offer great support for the efforts being made in the medical field to further develop NIPT and improve its efficacy on all levels. From a psychological perspective however, it still remains a priority that best ethical standards are maintained and practical efforts should be put in place for this purpose. Thoughts on this are addressed in the following section.

4.2. **What are the non-medical risks of the wider application of non-invasive tests?**

One area that has already received much research attention is related to ethical considerations regarding NIPT becoming more widely available. For example, the ease with which this test is delivered – through a blood draw – should not in any way compromise the level of genetic counselling and support that is provided to these women (Murdoch et al, 2016). There is concern that with already limited resources in genetic counselling and the absence of any medical risk associated with NIPT, protocols around communicating all the relevant information and potential outcomes to women prior to them accepting the test may be compromised due to the absence of any immediate threat (Menezes et al, 2013). It is, however, of utmost importance that medical staff remain aware of the importance of this and continue to thrive to elicit an informed decision from women whilst communicating key information and preparing them for the indirect risks that they may be exposed to (i.e. if NIPT indicates high risk for any of the three main chromosomal abnormalities it is currently used for, an invasive test – and thus a risk of miscarriage – would be required before a definitive diagnosis can be made).

One important factor to consider is that according to current clinical practices, even though women may be provided with some written information on screening and its purpose prior to having their first trimester combined test, they only receive genetic counselling after their individualised risk shows that they are at moderate or high risk. This means that when faced with an adverse result, women may already be in a heightened psychological state to be able to process new information rationally and arrive to an informed decision. Thus, they may become even more stressed and rely on others, such as their doctors or other external sources, to make their decision. Whilst NICE guidelines recommend that women be informed of the purpose of any screening procedure before it is carried out, it is unclear how much time is invested in the communication of potential outcomes and subsequent decisions that may lay ahead prior to women receiving their combined screening results (NICE, 2008). It would be interesting for future studies to explore the impact of informing all women prior to them receiving their results and how this may be beneficial or not for them. Might this expose women to a potential increase in anxiety levels because of the potential risks coming to the forefront of their minds? And if so, is this transient and balances out for those who then receive a “screen negative” result? Does having more information beforehand indeed allow women to assess their options more rationally without the added stress of a “screen positive” result already at hand? A longitudinal study where women’s knowledge of potential future options against their anxiety levels are assessed before and after receiving their combined screening results could potentially lead to changes in the current practice that may be in women’s best psychological interest. This would shed light on the current controversy within the literature whereby some have reported a lingering anxiety throughout pregnancy as a result of screening procedures highlighting the possibility of something being wrong with the foetus (Green et al, 2004), whilst others reporting a continuous decrease in anxiety during pregnancy in women who participated in screening (Lou, Mikkelsen, Hvidman, Petersen, & Nielsen, 2015). In addition, and in light of the introduction of NIPT into clinical practice, the 7-10 day turnaround period required for the results has also been associated with prolonged anxiety in women that usually, however, decreases

upon receipt of a negative result, yet in some cases remains elevated (Lewis et al, 2016). This may reflect a lack of faith in NIPT's reliability, an increased concern due to conflicting results between the combined screening test and NIPT, or simply a personality trait of heightened anxiety that may characterise some of the women; further research exploring this aspect would be of clinical importance as it could help guide health professionals as to how they can more efficiently counsel and support such women.

Another important element is ensuring the best communication methods are used that correspond to women's needs and preferences. When it comes to prenatal testing women are usually given a probabilistic number (i.e. 1/280) that is, however, not always easy to comprehend (Pighin, Bonnefon, & Savadori, 2011). Risk communication is undoubtedly a complex matter, but it might be that women are more able to understand a verbal explanation of the results (i.e. "not likely") especially in this context where emotions are highly involved (Timmermans, 2005). Future research should focus on identifying women's preferred method of risk communication and develop appropriate resources that will help health professionals on this sensitive subject.

Further to this, it is of utmost importance that health professionals involved in the prenatal diagnosis process are aware of how to accurately interpret NIPT test results. Considering the importance of informed decision making when it comes to medical issues (Brauer, 2015), and the extent to which women rely on their doctors for understanding the results (Hedrick, 2005) this is an area that requires the attention of policy makers and potentially hospital directors that are in charge of their staff training. While there are guidelines on how to use this test, there are no published guidelines on quality control and assurance, thus leaving a window for potential misuse and misinterpretation unless further measures are taken to prevent this from happening (Lutgendorf, Stoll, Knutzen, & Foglia, 2014). In addition, it has been highlighted by parents of children with Down's syndrome that in order for one to make an informed decision when it comes to prenatal testing it is important not only to be counselled about the test options and their implications but also about the condition they are being tested for and how it is, for example, to live with a child with Down's syndrome (van Schendel et al, 2016). Nonetheless, with NIPT being trialled for use with several different disorders it will become increasingly difficult for health professionals to provide such counselling to all parents, thus unveiling a potential disadvantage of the wider use of this test.

4.3. How will the wider use of NIPT affect the prenatal diagnostic practice?

Undoubtedly the development of NIPT was revolutionary for prenatal diagnosis practice and it is commonly acknowledged that it will continue to have a significant impact on current practice (Gil et al, 2014). As it continues to be improved in terms of accuracy and also in terms of the range of conditions it is able to detect, it is thought that it will also continue to rise in women's preference (Chetty, Garabedian, & Norton, 2013). There is, however, a continuing debate on which cases it will be more suitable for.

With a general understanding being that the cost of this will be unsustainable for the NHS to roll it out as a routine practice offered to all pregnant women, NIPT may be most appropriate for women falling in the intermediate risk category (1:2500). Therefore, it may be best suited as a half-way step that is offered to women in the moderate/high risk group between their combined screening and an invasive test. This would allow for a more accurate personalised estimated risk to be offered to women thus discriminating between those who are at a very high risk and those for whom even though present, the level of risk does not warrant the additional risk of miscarriage that would be associated with an invasive procedure. As a result, many women who would otherwise not have proceeded with any further test due to the associated risk now have a greater insight and can potentially gain further reassurance. On the other hand, those who would have instantly sought reassurance through an invasive test now also have the opportunity to minimise the risks by weighing up the pros and cons of getting a 100% result versus a 99%. In line with shared decision making that has been the advocated approach in medical decision making since the mid-1990s (Moumjid, Gafni, Bremond, & Carrere, 2007) it is important that health professionals and patients share both the process and the ownership of the decision outcome (Coulter, 1999). In other words, through genetic counselling women should get a clear understanding of the risk or severity of the condition being screened for, as well as the risks, benefits, and alternatives of the screening and diagnostic tests being offered; in addition, they should be given the time and space to weigh their personal values against the potential costs and benefits of the tests under offer and engage in decision-making to the extent that they feel comfortable with (Sheridan, Harris, & Wolf, 2004).

Nonetheless, even though the uptake of invasive tests has already significantly decreased following the introduction of NIPT (Gil et al, 2014), these are by no means to be removed from current prenatal diagnosis as they are the only means of getting a definitive diagnosis about the health of the foetus. One potential concern however, may have to do with the skill of doctors performing invasive tests being compromised due to lack of practice. This leads to the question: what effect will the introduction of NIPT have on the procedure-related risk of miscarriage? At the moment this is reported to be approximately 1% (Hill et al, 2012) depending on the skill of the clinician, and an undesirable outcome of the infrequency of their performance would be an increase in this risk. This may see invasive diagnostic tests becoming the object of more highly specialized professionals who have the level of skill required to perform such a high-risk procedure, but it is important for all health professionals in this field to be mindful of such potential downfalls and thus incorporate measures within their practice to prevent this from happening. This could involve all new doctors being required to assist and perform a certain amount of invasive diagnostic procedures under the supervision of an experienced consultant as part of their training and that this also be regularly sustained through internal clinical skills workshops. It is important to minimize the risks posed to any pregnancy and the development of non-invasive tests is definitely a step in the right direction. However, with invasive tests still being an integral part of the process involving high-risk cases, it is important not to let it fade in the back with more serious consequences for those who still have to go through it.

4.4. How do women choose?

In terms of the primary research question there are some important findings to draw on. Firstly, as far as invasive tests are concerned none of the psychological factors under investigation played a significant role in women's decision making process. It seems that a negative attitude to medicine and a positive attitude to prenatal tests increase the likelihood of a woman having an invasive test whereas a greater level of anxiety has the contrary effect with such women being less likely to choose this type of test. Possible explanations for these findings have been discussed earlier in Chapter 3 but it is important to note that while these factors may have played some role and could potentially be further explored in future research, they did not reach statistical significance.

On the contrary, as far as NIPT is concerned, some psychological factors were found to significantly contribute to a woman's decision: a negative attitude to doctors and an internal locus of control increase the likelihood of a woman choosing to have a non-invasive test whereas a negative attitude to medicine decreases her chances.

In considering all the above findings together, a consistent finding seems to revolve around negative attitudes towards medicine that seem to shape women's decision at least to some extent one way or the other: while it drives them in the direction of invasive tests, it averts them from non-invasive tests. The most obvious explanation for this would be that despite being negatively biased towards medicine in general, when it comes to the serious matter of their unborn baby's well-being women are still willing to put their faith into long-standing and well-established procedures, whilst being more critical towards newly developed tests. This is important in that it means these women may be posing themselves at a greater risk that is associated with invasive procedures without really making the best of medical technology's rapid advances. It may be that this particular population, predisposed by their own conceptions about medicine or technology advancements, do not seek information on new methods of prenatal testing and diagnosis and thus, are more ignorant of the real costs and benefits of such procedures. Whilst it was originally intended to include knowledge of prenatal tests as a variable in the questionnaire developed for this study, items relating to it were dropped during the factor analysis process and thus 'knowledge' was not assessed in relation to women's decision making processes. Therefore it is difficult to draw safe conclusions and further research is required to explore this further. Nonetheless, it could still be argued that while it may be easier to trust a medical procedure that has been around for years, it may be useful for particular attention to be paid to these women – especially if future studies identify a more limited knowledge-base - in educating them about the new non-invasive test and thus enabling them to come to a truly balanced and informed decision. This is in line with ongoing research regarding technology acceptance which has been defined as '*the approval, favourable reception and ongoing use of newly introduced devices and systems*' (Ziefle & Schaar, 2011). Evidence suggests a general distrust towards medical technology, and women in particular perceiving the value of medical technology as lower than men as they tend to focus more on the 'costs' versus the 'benefits' of using such methods (Ziefle & Schaar, 2011). Therefore, it may be that women

attending their appointment for their first trimester combined screening test will have to be approached in a more sensitive manner so as not to further alienate them and the information will have to be communicated to them in a simple manner that is sharp enough to engage their attention and ensure they have a clear understanding of both the benefits and the costs of any test that is being offered to them. A focus group interview with such women would help in identifying what the best means of communicating this information might be as well as exploring what key cognitions may play in their mind affecting their attitudes and beliefs. This would enable health professionals to initially assess their acceptability towards new medical information and subsequently develop an appropriate intervention so as to tailor information to the needs of these women.

Another important finding that significantly contributed to women's choice of NIPT but which was also found to have a large effect size on women's decision to have an invasive test (although not statistically significant) was internal locus of control. It appears that women who believe they have greater control over their health are more likely to have some sort of test whereas those with a chance locus of control were found to be more likely to choose no further testing. This again, shifts our attention to the beliefs women hold about the controllability of a condition and what it is that actually shapes this belief. While this is consistent with some previous studies (Lumley et al, 2006) and may be explained by women viewing screening and testing as a proactive health behaviour, there are still conflicting findings within the wider literature (Furr & Seger, 1998) indicating that further research is required before drawing firm conclusions. As discussed in Chapter 3, a more pregnancy-related measure of locus of control such as the Fetal Health Locus of Control Scale (FHLC; Labs & Wurtele, 1986) that has long been developed but has only been used in one study relating to prenatal testing (Turrieff-Jonnason, 2004) would be of interest to be further explored along these lines as it could provide useful insight to women's feelings of controllability over the health of their baby. Should further support for the contribution of internal locus of control be established, this would provide grounds for appropriate interventions to be developed that will aim to empower women so as to facilitate a greater sense of control and thus potentially a more proactive role in their antenatal care decisions.

In relation to the above, the role of others in women's decision making process regarding uptake of prenatal tests, seems to also warrant further exploration. The general indication in the wider literature so far, is that partners are the most influential on women's decision-making process, followed by family and friends (Georgsson et al, 2016). However, prior research has also shown that women tend to go along with their partner's opinion in the case of a disagreement (Garcia et al, 2008) and therefore this might mean that they do not necessarily make a decision that is in line with their own values and attitudes. The impact on this on their psychological well-being is unknown, especially if the pregnancy outcome is not optimal, and therefore efforts should be put into ensuring that all women are making informed decisions when it comes to prenatal testing. This may mean involving the partners more in the whole process so as to ensure that both parties have all the necessary information required prior to making such a decision and also opening the lines of communication between them so as to

facilitate a mutual deliberation and decision making process. More research involving partners is required in order to shed light on this front.

Finally, probably the most important finding of this study was that when personalised risk based on the first trimester combined screening test was included in the model, all psychological and socio-demographic factors became insignificant and this was the single factor that influenced women's decision making process. As far as invasive tests are concerned a high risk for T21 was the only significant predictor whereas for non-invasive tests a high risk for both, T13/T18 and T21, were significantly related to decision outcome. This was a prospective study, with data being collected prior to women finding out their risk status, thus indicating that further research on women after being informed of their risk status would be warranted. What happens to them, emotionally and cognitively, when they are actually informed of a threatening outcome? Is their locus of control, for example, completely wiped out rendering them more vulnerable to what now may seem out of their control? How are their attitudes towards doctors and medicine affected? Do they find themselves becoming more open to tests in hope of a reassuring result? Future studies aiming to answer these questions would be of clinical importance as they would allow relevant tools to be developed so as to compliment the communication of risk results and facilitate adjustment to the news and a comprehensive processing of the information thus enabling an informed decision regarding further action. A recent study that was published after the analysis of our data (Beulen et al, 2016), reported that a web-based decision aid facilitates autonomous informed decision when it comes to prenatal testing and therefore further exploration along these lines or other effective resources may be appropriate.

4.5. **What about “low-risk” women?**

So far it has been clear that most of the attention has been focused on women identified as being at intermediate or high risk of having a baby with a chromosomal abnormality and how to best support them in their decisions. But in adopting a more holistic view of our findings another striking outcome could be that all women who were low risk on both T21 and T13/T18 opted for no further testing at all. While this may have been a result of them not being directly offered the choice by their medical team, it also suggests that having a reassuring outcome from the combined screening test is enough confirmation for women to not want to seek further reassurance. While this is important in that it does not expose these women to any risk of iatrogenic miscarriage it does not necessarily mean that women in this category do not experience any anxiety or feel completely reassured by their screening results. It would be interesting to explore these women's feelings following a “screen-negative” result and how they understand this finding. Notably, the combined test detects approximately 85-90% of Down Syndrome pregnancies with a 4.2% false positive rate (Alfirevic & Neilson, 2004) and therefore it is possible that even in the event of a normal result a woman may still be carrying a baby with Down's Syndrome. Women are informed of this likelihood and evidence suggests that they have the ability to use personalized screening information in making a scientifically and ethically rational decision about invasive testing (Nicolaidis, Chervenak, McCulloch, Avgidou, & Papageorgiou, 2005). However, little research has been done to explore how much this

screening affects their emotional state. This is not to suggest that invasive tests should be offered or carried out on all women but certainly highlights the contribution of NIPT that offers close-to-diagnostic results without any risks.

However, at this point in time at least, it is not within screening policy to offer NIPT to all women as this would incur significant costs on the NHS without being considered absolutely necessary, and therefore some could argue it casts this group of women at a slightly disadvantageous position. It is encouraging, however, that evidence supports the effectiveness of non-invasive prenatal testing on a routinely screened first trimester population (Nicolaides et al, 2012) suggesting that even if not routinely offered it may still be a better option than directly having an invasive test for women who still wish to have further reassurance despite receiving a “screen-negative” result from their combined screening.

From a Health Psychology perspective, it is important to ensure that equal psychological support is in place for all pregnant women regardless of their combined screening results. With pregnancy itself, regardless of prenatal screening tests, being associated with psychological stress and anxiety in many women (Statham, Green, & Katesios, 1997), it is likely that undergoing tests for the identification of any abnormality may increase women’s anxiety and concerns by bringing to the forefront of their mind the potential adverse outcomes. But how truly reassured are women after receiving a “low-risk” result? Whilst there is some evidence to suggest that early screening for Down’s syndrome by means of ultrasound does not increase women’s anxiety in the second trimester and two months post-delivery (Ohman, Saldvedt, Grunewald, & Waldenstrom, 2004), it is observed that most studies focus on women receiving an adverse result and therefore more longitudinal studies in the UK targeting women with a normal outcome, would be warranted in order to explore the impact of the combined test and therefore determine the level of support that is required for this population.

It is important to note that in the present study anxiety levels at baseline measurement (prior to combined screening test results) were relatively stable across all women indicating that there may not be much variation in women’s anxiety response prior to being informed about their results. The mean levels were 5.33 and 5.43 in low and moderate/high risk groups respectively which according to the recommended cut-off point of 8 for the anxiety scale (HADS questionnaire) does not indicate clinical anxiety. While positive in terms of women’s emotional well-being, it would have been interesting to also measure their anxiety levels post-results in order to assess the impact of the screening and how being ascribed a personalized risk may have affected them.

4.6. Strengths & Limitations

Despite the important findings, this study is not without limitations. First of all, the methodology – which was questionnaire-based- may have been restrictive in terms of identifying potential factors that influence women’s decision-making process. An attempt to prevent this restrictive nature of data collection was made by including an open-ended question where women were asked to disclose the key factors affecting their choice. However, even though this provided

some further insight, it would have been even more insightful to include some interviews, either individual or in the form of focus groups, in our data collection process where women would have the opportunity to expand on their thoughts and potentially reveal more aspects that could not be captured in the limited space of one open-ended question.

In addition, there were several factors that we originally set out to explore, yet these were rejected during the factor analysis in the pilot study. Such factors include knowledge and the influence of important others (subjective norms), that have been reported in the literature with conflicting findings (Michie et al, 2002) and therefore require further investigation especially since the addition of NIPT into clinical practice. However, a strength to counter-balance this, was that a holistic approach was adopted where a combination of different models was used to guide the development of our questionnaire, thus not limiting the scope of the factors explored to one set of variables.

Another potential limitation is that the original scope of the study was to explore women's decision making process regarding the uptake of invasive diagnostic tests and therefore the pilot study was mainly focused on amniocentesis and CVS. With the introduction of NIPT in the clinical practice of our research site, however, it was considered plausible to expand the scope of our study so as to additionally include NIPT. It was thought that this would provide more interesting and useful clinical/research information considering the changes that will inevitably occur in the field of prenatal diagnosis with the increasing use of NIPT, especially since there are talks about rolling it out in the NHS (Morris, Karlsen, Chung, Hill, & Chitty, 2014).. It is important to note, that following our decision to expand the original scope of the study appropriate amendments were made to the questionnaire so as to include NIPT as well and these were approved by the Stamford National Research Ethics Committee prior to conducting our main study. Nonetheless, some of the questions had to be somewhat more generalised following these changes, i.e., looking at attitudes towards prenatal testing rather than attitudes towards invasive vs. non-invasive procedures. A more targeted approach may have clarity to the differences between the two different testing methods and would be of use to be explored by future studies.

Having said this, a strength of our study is that it was prospective and therefore explored women's intentions to take up a particular test which was then confirmed or disconfirmed by following up with her final decision. This could have been further improved by follow-up interviews where women would have the opportunity to reflect on their original intentions and actual behaviour as well as on what else may have ended up affecting their decision if this was changed after the receipt of a screen-positive result. This would provide insight to the everlasting debate in the literature as to how much intentions predict actual behaviours.

Moreover, another limitation is the small sample size in high-risk women and women choosing to have an invasive test. This is justified, however, by the nature of our study and a strength of the study to offset this drawback is that a special statistical method was used that is applicable

to such cases (rare events such as being at high risk) and thus allowing for the detection of significant results even in the event of unequal sample sizes.

Finally, the fact that our study was based only on one research site limits the generalisability of the findings. Further research on multiple sites would allow for more firm conclusions to be drawn and also allow for greater variability in the population being tested. This may also lead to different findings in terms of religious and socio-cultural influences on women's decision making process that has been suggested before but was not evident in this study, or indeed confirm that these factors do not ultimately determine women's choices.

Whilst all the above points are to be considered in the context of our current findings, this study offers important information for future clinical and research use on a topic that is now expanding, in light of the changes that are currently under way in the prenatal diagnosis scene.

4.7. Concluding remarks

This study was one of the first to address women's decision making processes in relation to prenatal diagnosis including the new non-invasive NIPT test. Unsurprisingly low-risk women opted for no further testing but moderate and high risk women predominantly opted for NIPT with some exceptions of high risk cases seeking the definitive diagnosis of the invasive tests. This is thought to be representative of the general population as seen through initial evidence (Gil et al, 2015) and indicates a major shift in prenatal diagnosis as it was practiced until now. With NIPT becoming more widely available and the uptake of invasive tests reducing, it is important for Health Professionals to keep in mind the potential ethical and practical drawbacks whilst maintaining as their priority that an informed decision is made on behalf of women.

Whilst attitudes towards medicine, internal locus of control, and the role of partners are all areas that would warrant further research, if there was one key finding that overrules the rest is that when personalized risk estimate based on the first trimester combined screening is included in the model then this forms the single predictor of women's decision. Therefore, it may be more appropriate that greater attention is focused on risk communication and doctor-patient relationship. If finding out their risk level is going to play such a significant role in women's decision, it is of utmost importance that this is communicated to them in a sensitive and easily-comprehensible manner whilst also encouraging an open communication whereby women feel comfortable raising their concerns with their healthcare professionals. This is something that should be encouraged in all practices as a means of empowering women to gather the information they need from reliable sources that can also be complimented by other means such as the recommendation of particular websites by their healthcare team. Through this continuous growth in the doctor-patient communication it is hoped that a smooth process will be facilitated in an otherwise inevitably complex and emotionally-laden situation.

5. References

- Aalfs, C. M., Oort, F., J., Haes, H., Leschot, N.J., & Smets, M.A. (2006). Counselor-counselee interaction in reproductive genetic counseling: does a pregnancy in the counselee make a difference? *Patient Education and Counseling*, 60, 80-90.
- Abdi, H., & Williams, L.J. (2010). Principal component analysis. *Wiley Interdisciplinary Reviews: Computational Statistics*, 2, 433-459.
- Abu-Musa, A.A., Nassar, A.H., & Usta I.M. (2008). Attitude of women with IVF and spontaneous pregnancies towards prenatal screening. *Human Reproduction*, 23(11), 2438-2443.
- ACOG (2012). Noninvasive prenatal testing for fetal aneuploidy: Committee opinion No 545.
- Ahman, A., Runestam, K., & Sarkadi, A. (1991). Did I really want to know this? Pregnant women's reaction to detection of a soft marker during ultrasound screening. *Patient Education and Counseling*, 81, 87-93.
- Ahmed, S., Ahmed, M., Sharif, S.M., Sheridan.E., & Taylor (2012). Attitudes towards prenatal testing and termination of pregnancy in British Pakistani parents and relatives of children with recessive conditions in the UK. *Prenatal Diagnosis*, 32, 954-959.
- Ahmed, S., Bryant, L.D., Tizro, Z., & Schickle, D. (2012). Interpretations of informed choice in antenatal screening: A cross-cultural, Q-methodology study. *Social Science & Medicine*, 74, 997-1004.
- Ajzen I. (1991). The Theory of Planned Behavior. *Organizational Behavior and human decision processes*. 50, 179-211.
- Ajzen, I. (1991). The theory of planned behavior. *OrganBehavHumDecis Process*, 50, 179–211.
- Alberman, E., Huttly, W., Hennessy, E., & McIntosh, A. (2003). The use of record linkage for auditing the uptake and outcome of prenatal serum screening and prenatal diagnostic tests for Down Syndrome. *Prenatal Diagnosis*, 23, 801-806.
- Alfirevic Z. & Walkinshaw S.A. (2010). Amniocentesis and Chorionic Villous sampling, *RCOG Green Top Guideline*. & Guideline No 8.
- Alfirevic, Z. & Neilson, J.P. (2004). Antenatal screening for Down's syndrome: Nuchal translucency plus biochemical tests has the lowest false positive rate. *BMJ*, 329, 811-812.

Alfirevic, Z., Gosden, C.M., & Neilson, J.P. (2000). Chorion villus sampling versus amniocentesis for prenatal diagnosis. *Cochrane Database Syst Rev*, 2:CD000055.

Alkazaleh, F., Thomas, M., Grebenyuk, L., Glaude, L., Savage, D., Johannesen, J., Caetano, M., & Windrim, R. (2004). What women want: women's preferences of caregiver behavior when prenatal sonography findings are abnormal. *Ultrasound Obstet Gynecol*, 23, 56-62.

Allyse, M., Sayres, L.C., Goodspeed, T.A., & Cho, M.K. (2014). Attitudes towards non-invasive prenatal testing for aneuploidy among US adults of reproductive age. *Journal of Perinatology*, 34, 429-434.

Allyse, M., Sayres, L.C., King, J.S., Norton, M.E. and Cho, M.K. (2012). Cell-free fetal DNA testing for fetal aneuploidy and beyond: clinical integration challenges in the US context. *Human Reproduction*, 27(11), 3123-3131.

American College of Obstetricians and Gynecologists (ACOG) (2007). Screening for fetal chromosomal abnormalities. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); ACOG practice bulletin, no.77.

American College of Obstetricians and Gynecologists (ACOG) Committee on Genetics (2012). Committee opinion no. 545. Noninvasive prenatal testing for fetal aneuploidy. *Obstetrics and Gynecology* 120(6): 1532–4.

American College of Obstetricians and Gynecologists (ACOG), 2012. Non-invasive prenatal testing for fetal aneuploidy. Committee opinion No.545. *Obstetrics & Gynecology*, 120(6), 1532–1534.

Anderson, G. (1999). Nondirectiveness in prenatal genetics: Patients read between the lines. *Nursing Ethics*, 6, 126–136.

Anderson, G. & Brown, C. (2009). Fetal chromosomal abnormalities: antenatal screening and diagnosis. *American Family Physician*, 79(2), 117-123.

Anderson, J., Rainey, M., & Eysenbach, G. (2003). The impact of cyberhealthcare on the physician-patient relationship. *Journal of Medical Systems*, 27(1), 67-84.

Anderson, L.A., DeVellis, R.F., Boyles, B., & Feussner, J.R. (1989). Patients' perceptions of their clinical interactions: development of the multidimensional desire for control scales. *Health Education Research: Theory & Practice*, 4(3), 383-397.

Antenatal care: routine care for the healthy pregnant woman, NICE Clinical Guideline (March 2008).

- Asch, A. (1999). Prenatal diagnosis and selective abortion: a challenge to practice and policy. *Am J Public Health*, 89, 1649–1657.
- Ashoor, G., Syngelaki, A., Wagner, M., Birdir, C. and Nicolaides, K.H. (2012). “Chromosome-selective sequencing of maternal plasma cell-free DNA for first-trimester detection of trisomy 21 and trisomy 18,” *American Journal of Obstetrics & Gynecology*, vol. 206, no. 4, pp. 322.e1–322.e5.
- Ashoor, G., Syngelaki, A., Wang, E., Struble, C., Oliphant, A., Song, K., & Nicolaides, K. (2013). Trisomy 13 detection in the first trimester of pregnancy using a chromosome-selective cell-free DNA analysis method. *Ultrasound Obstet Gynecol*, 41, 21-25.
- Baig S., Ho S.S.Y., Ng B.L., Chiu L., Koay E.S.C., Leow G.H., Gole L., Kothandaraman N., Chan J., Sun X., Chan Y.H., Rauff M., Su L.L., Biswas A., & Choolani M. (2010). Development of quantitative-fluorescence polymerase chain reaction for the rapid prenatal diagnosis of common chromosomal aneuploids in 1,000 samples in Singapore. *Singapore Med J* 51(4), 343-348.
- Bandura A. (1977). Social Learning Theory. Englewood Cliffs, New Jersey: Prentice-Hall.
- Barrett, A., Advani, H.V., Chitty, L.S., & Choolani, M. (2016). Evaluation of preferences of women and healthcare professionals in Singapore for implementation of noninvasive prenatal testing for Down Syndrome. *Singapore Medical Journal*, doi:10.11622/smedj.2016/14.
- Bartels, D.M., Leroy, B.S., McCarthy, P., & Caplan, A.L. (1997). Nondirectiveness in genetic counseling: a survey of practitioners. *Am J Med Genet*, 72, 172–179.
- Bauer, A. (2011). Factors influencing decision-making in prenatal screening for Down Syndrome. A paper presented to the faculty of The University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Public Health in the Department of Maternal and Child Health.
- Beaumont, 2012. An introduction to Principal Component Analysis & Factor Analysis Using SPSS 19 and R.
- Beck, U. (1992). From Industrial Society to the Risk Society: Questions of Survival, Social Structure and Ecological Enlightenment. *Theory, Culture and Society*, 9 (1), 97-123.
- Becker, M.H., Kaback, M.M., Rosenstock, I.M., & Ruth, M.V. (1975). Some influences on public participation in a genetic screening program. *Journal of Community Health*, 1(1), 3-14.
- Bekker, H.L., Hewison, J., & Thornton, J.G. (2003). Understanding why decision aids work: linking process and outcome. *Patient Educ Couns*, 50, 323–329.

Benn, P., Borell, A., Chiu, R., Cuckle, H., Dugoff, L., Faas, B., Gross, S., Johnson, J., Maymon, R., Norton, M., Odibo, A., Schielen, P., Spencer, K., Huang, T., Wright, D., & Yaron, Y. (2013). Position statement from the aneuploidy screening committee on behalf of the board of the International Society for Prenatal Diagnosis. *Prenatal Diagnosis*, 33(7), 622-629.

Benn, P., Cuckle, H., & Pergament, E. (2013). Non-invasive prenatal testing for aneuploidy: current status and future prospects. *Ultrasound Obstet Gynecol*, 42, 15-33.

Benn, P.A. & Chapman, A.R. (2010). Ethical challenges in providing non-invasive prenatal diagnosis. *Curr Opin Obstet Gynecol*, 22, 128–134.

Bennett, R. (2001) Antenatal genetic testing and the right to remain in ignorance, *Theory in Medical Bioethics*, 22, 461–71.

Berkenstadt, M., Shiloh, S., Barkai, G., Katznelson, M., & Goldman, B. (1999). Perceived Personal Control (PPC): A new concept in measuring outcome of genetic counseling. *American Journal of Medical Genetics*, 82, 53-59.

Berland, G.K., Elliott, M.N., Morales, L.S., Algazy, J.L., Kravitz, R.L., Broder, M.S., Kanouse, D.E., Munoz, J.A., Puyol, J.A., Lara, M., Watkins, K.E., Yang, H., & McGlynn, E.A. (2001). Health information on the internet: Accessibility, quality, and readability in English and Spanish. *JAMA*, 285(20), 2512-2621.

Bertaux, D. (1981). From the life-history approach to the transformation of sociological practice. In Daniel Bertaux (Ed.), *Biography and society: The life history approach in the social sciences* (pp.29-45). London: Sage.

Beulen, L., van den Berg, M., Faas, B.H.W., Feenstra, I., Hageman, M., van Vugt, J.M.G., & Bekker, M.N. (2016). The effect of a decision aid on informed decision-making in the era of non-invasive prenatal testing: a randomised controlled trial. *European Journal OF Human Genetics*, 24, 1409-1416.

Bianchi, D.W., Oepkes, D., & Ghidini, A. (2013). Current controversies in prenatal diagnosis 1: should noninvasive DNA testing be the standard screening test for Down syndrome in all pregnant women? *Prenatal Diagnosis*, 33, 1-6.

Bijma, H.H., Van der Heide, A., Wildschut, H.I.J., Van der Maas, P.J., & Wladimiroff, J.W. (2007). Impact of decision-making in a multidisciplinary perinatal team. *Prenatal Diagnosis*, 27, 97-103.

Bjelland, I., Dahlb, A.A., Haug, T.T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *Journal of Psychosomatic Research*, 52(2), 69–77.

- Bodegird, G., Fyro, K., & Larsson, A. (1988). Psychological reactions in 102 families with a newborn who has a falsely positive screening test for congenital hypothyroidism, *Acta Paediatr. Scand., suppl304*, 3-21.
- Bountziouka, V. & Panagiotakos, D.B. (2012). The Role of Rotation Type used to Extract Dietary Patterns through Principal Component Analysis, on their Short-Term Repeatability. *Journal of data science*, 10, 19-36.
- Brajenović-Milić, B., Babić, I., Ristić, S., Vraneković, J., Brumini, G., & Kapović, M. (2008). Pregnant women's attitudes toward amniocentesis before receiving Down's syndrome screening results. *Women's Health Issues*, 18(2), 79-84.
- Brauer, S. (2015). Moral implications of obstetric technologies for pregnancy and motherhood. *Med Health Care and Philosophy*, 1-10.
- Bricker, L., Garcia, J., & Henderson, J. (2000). Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. *Health Technology Assessment*, 4(16), 1-193.
- Broom, A. (2005). Virtually healthy: the impact of internet use on disease experience and the doctor-patient relationship. *Qualitative Health Research*, 15(3), 325-345.
- Browner, C.H. & Preloran, H.M. (1999). Male partners' role in Latinas' amniocentesis decisions. *Journal of Genetic Counseling*, 8(2), 85-108.
- Bryant, L.D., Green, J.M., & Hewison, J. (2010). The role of attitudes towards the targets of behaviour in predicting and informing prenatal testing choices. *Psychology and Health*, 25(10), 1175-1194.
- Bushby K., Finkel R., Birnkrant D.J., Case L.E., Clemens P.R., Cripe L., Kaul A., Kinnett K., McDonald C., Pandya J., Poysky J., Shapiro F., Tornezsko J., & Constantin C. (2010). Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. *The Lancet*, 9, 77-90.
- Campbell, J.D., Stanford, J.B., & Ewigman, B. (1996). The social pregnancy interaction model: conceptualizing cognitive, social and cultural barriers to prenatal care. *Applied Behavioral Science Review*, 4(1), 81-87.
- Carroll, J.C., Brown, J.B., Reid, A.J., & Pugh, P. (2000). Women's experience of maternal serum screening. *Canadian Family Physician*, 46, 614-620.
- Cattell, R. B. (1966). The scree test for the number of factors. *Multivariate Behavioral Research*, 1, 245-276.

Cattell, R. B. (1978). *The scientific use of factor analysis in behavioral and life sciences*. New York: Plenum. Cattell, R. B., & Dreger, R. M. (Eds.)

Cederholm, M., Axelsson, O., & Sjoden, P.O. (1999). Women's knowledge, concerns and psychological reactions before undergoing an invasive procedure for prenatal karyotyping. *Ultrasound Obstetrics and Gynecology*, 14, 267-272.

Cederholm, O.A. & Sjoden, P.O. (1999). Women's knowledge, concerns and psychological reactions before undergoing an invasive procedure for prenatal karyotyping. *Ultrasound Obstet Gynecol*, 14, 267-272.

Chen, L.S. & Goodson, P. (2007). Factors affecting decisions to accept or decline cystic fibrosis carrier testing/screening: a theory-guided systematic review. *Genetics in Medicine*, 9(7), 442-450.

Chetty, S., Garabedian, M. J., & Norton, M. E. (2013). Uptake of noninvasive prenatal testing (NIPT) in women following positive aneuploidy screening. *Prenatal diagnosis*, 33(6), 542-546.

Chitty, L.S., Hill, M., White, H., Wright, D., & Morris, S. (2012). Noninvasive prenatal testing for aneuploidy – ready for prime time? *American Journal of Obstetrics and Gynecology*, 269-275.

Christianson A.L., Howson C.P., & Modell B. (2006). *March of Dimes Global Report on birth defects: the hidden toll of dying and disabled children*. March of Dimes Birth Defects Foundation, White Plains, New York, USA (Available online at: www.marchofdimes.com).

Clare Williams, C., Alderson, P., & Farsides, B. (2002). Too many choices? Hospital and community staff reflect on the future of prenatal screening. *Social Science & Medicine*, 55, 743-753.

Clarke, A. (1997). The process of genetic counselling. In Harper, P. & Clarke, A. (Eds.), *Genetics, society and clinical practice* (pp. 179–200). Oxford: BIOS Scientific Publishers.

Cohen, J. (1962). The statistical power of abnormal-social psychological research: A review. *Journal of Abnormal and Social Psychology*, 65, 145-153.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Erlbaum.

Cole, P. (1979). The evolving case-control study. *J Chronic Dis*, 32, 15-27.

- Conner, M. & Norman, P. (1994). Comparing the health belief model and the theory of planned behaviour in health screening. In D. R. Rutter and L. Quine (Eds), *Social Psychology and Health: European Perspectives*, pp. 1-24. Aldershot: Avebury.
- Conroy, R.M., Teehan, M., Siriwardena, R., Smyth, O., McGee, H.M., & Fernandes, P. (2002). Attitudes to doctors and medicine: the effect of setting and doctor-patient relationship. *Journal of Health Psychology*, 7, 117-125.
- Coulter A. (1999). *Shared decision-making: a summary and future issues*. In: Maslin, A.M., Powles, T.J., eds. *Breast Cancer: Sharing the decision*. Oxford, UK: Oxford University Press.
- Creswell, J. (1998). *Qualitative inquiry and research design: Choosing among five traditions*. Thousand Oaks, CA: Sage.
- Dahl, K., Hvidman, L., Jorgensen, F.S., & Kesmodel, U.S. (2011). Knowledge of prenatal screening and psychological management of test decisions. *Ultrasound Obstet Gynecol*, 38, 152-157.
- Daniilidis, A., Karydas, J., Zournatzi, V., Tantanasis, T., Giannoulis, C., & Tzafettas, J. (2008). A four-year retrospective study of amniocentesis: one centre experience. *Hippokratia*, 12(2), 113-115.
- Davies, B.L. & Doran, T.A. (1982). Factors in a woman's decision to undergo genetic amniocentesis for advanced maternal age. *Nursing Research*, 31(1), 56-59.
- Davis-Floyd, R.E. (1994). The Technocratic Body: American Childbirth as Cultural Expression. *Social Science & Medicine*. 38(8), 1125-1140.
- Davis-Floyd, R.E. (2001). The Technocratic, Humanistic, and Holistic Paradigms of Childbirth. *International Journal of Gynecology & Obstetrics*, 75, S5-S23.
- Davison, A., Barns, I., & Schibeci, R. (1997). Problematic publics : A critical review of surveys of public attitudes towards biotechnology. *Science, Technology and Human Values*, 22, 317-348.
- De Jong, A., Dondorp, W.J., Die-Smulders, C., Frints, S., & de Wert, G. (2010). Non-invasive prenatal testing: ethical issues explained. *European Journal of Human Genetics*, 18, 272-277.
- Devellis, B. M., Blalock, S. J. and Sandler, R. S. (1990), Predicting Participation in Cancer Screening: The Role of Perceived Behavioral Control. *Journal of Applied Social Psychology*, 20, 639-660.
- Diaz, J., Griffith, R., Reinert, S., Friedmann, P., & Moulton, A. (2002). Patients' use of the internet for medical information. *Journal of General Internal Medicine*, 17, 180-185.

- Dixon, A.M. (1994). The need for greater patient awareness in routine antenatal ultrasound. *Radiography Today*, 60(684), 9–11.
- Dormandy, E., Michie, S., Hooper, R., & Marteau, T.M. (2005). Low uptake of prenatal screening for Down Syndrome in minority ethnic groups and socially deprived groups: a reflection of women's attitudes or a failure to facilitate informed choices? *International Journal of Epidemiology*, 34, 346–352.
- Dormandy, E., Michie, S., Hooper, R., & Marteau, T.M. (2006). Informed choice in antenatal Down syndrome screening: a cluster-randomised trial of combined versus separate visit testing. *Patient Education and Counselling*, 61, 56–64.
- Dumit, J., & Davis-Floyd, R. (2000). Children of the third millennium. In R. Davis-Floyd, & J. Dumit (Eds.), *Cyborg babies* (pp. 1–20). New York: Routledge.
- Ehrenreich, B., & English, D. (1978). *For her own good: 150 years of experts' advice to women*. New York: Anchor Books.
- Elwyn G., Gray J., & Clarke A. (2000). Shared decision-making and non-directiveness in genetic counselling. *Journal of Medical Genetics*, 37, 135–138.
- Elwyn, G., Edwards, A., & Kinnersley, P. (1999). Shared decision-making in primary care: the neglected second half of the consultation. *British Journal of General Practice*, 49, 477–482.
- Elwyn, G., Gray, J., & Clarke, A. (2000). Shared decision-making and non-directiveness in genetic counselling. *J Med Genet*, 37, 135–138.
- Erdfelder, E., Faul, F., & Buchner, A. (1996). GPOWER: A general power analysis program. *Behavior research methods, instruments, & computers*, 28(1), 1–11.
- Everett, T. R., & Chitty, L. S. (2015). Cell-free fetal DNA: the new tool in fetal medicine. *Ultrasound in Obstetrics & Gynecology*, 45(5), 499–507.
- Everett, T.R. & Chitty, L.S. (2014). Cell-free fetal DNA: The new tool in Fetal Medicine. *Ultrasound in Obstetrics & Gynecology*, in press.
- Eysenbach, G. & Diepgen, T.L. (1998). Towards quality management of medical information on the internet: evaluation, labeling, and filtering of information. *BMJ*, 317(7171), 1496–1500.
- Eysenbach, G., Powell, J., Kuss, O., & Sa E.U. (2002). Empirical studies assessing the quality of health information for consumers on the world wide web. *JAMA*, 287(20), 2691–2700.
- Fajnzylber, E., Hotz, V.J., & Sanders, S.G. (2010). An economic model of amniocentesis choice. *Advances in Life Course Research*, 15, 11–26.

- Fang, C.Y., Dunkel-Schetter, C., Tatsugawa, Z.H., Fox, M.A., Bass, H.N., Grody, W.W. (1997). Attitudes toward genetic carrier screening for cystic fibrosis among pregnant women: the role of Health Beliefs and avoidant coping style. *Women's Health: Research on gender, behavior and policy*, 3(1), 31-51.
- Farrell, R.M., Agatista, P.K., Mercer, M.B., Smith, M.B., & Phillipson, E. (2015). Balancing risks: the core of women's decisions about noninvasive prenatal testing. *AJOB Empirical Bioethics*, 6(1), 42-53.
- Farrell, R.M., Hawkins, A., Barragan, D., Hudgin s, L., & Taylor, J. (2015). Knowledge, understanding, and uptake of non-invasive prenatal testing among Latina women. *Prenatal Diagnosis*, 35(8), 748-753.
- Fasouliotis, S.J., & Schenker, J.G. (2000). Maternal-fetal conflict. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 89, 101-107.
- Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods*, 41, 1149-1160.
- Feise, R. (2002). Do multiple outcome measures require p-value adjustment? *BMC Med Res Methodol*, 2(1). <http://dx.doi.org/10.1186/1471-2288-2-8>
- Ferres, M.A., Lichten, L., Sachs, A., Lau, K., & Bianchi, D. (2014). Rate of diagnostic procedures foraneuploidy in the post non-invasive DNA testing (NIDT) era. *PrenatDiagn*, 34(Suppl 1), 53.
- Field, A. (2000). *Discovering Statistics using SPSS for Windows*. London – Thousand Oaks – New Delhi: Sage publications.
- Field, A. (2013). *Discovering statistics using IBM SPSS Statistics*. London: Sage Publications.
- Firth, D. (1993). Bias reduction of maximum likelihood estimates. *Biometrika*, 80, 27–38.
- Fisher, W. A. (1984). Predicting contraceptive behaviour among university men: The role of emotions and behavioural intentions. *Journal of Applied Social Psychology*, 14, 104-123.
- Fiske, S.T. & Taylor, S.E. (1984). *Social Cognition*. Random House: NewYork.
- Fletcher, J., Hicks, N.R., & Boyd, P.A. (1995). Using decision analysis to compare policies for antenatal screening for Down's syndrome. *British Medical Journal*, 311, 351-356.
- Fox, S. & Duggan, M. (2013). Pew Internet & American Life Project, January 15, 2013. URL <http://pewinternet.org/Reports/2013/Health-online.aspx> accessed on 21February 25, 2015

- France, E.F., Wyke, S., Ziebland, S., Entwistle, V.A., & Hunt, K. (2011). How personal experiences feature in women's accounts of use of information for decisions about antenatal diagnostic testing for foetal abnormality. *Social Science & Medicine*, 72, 755-762.
- Fransen, M.P., Wildschut, H.I.J., Vogel, I., Mackenbach, J.P., Steegers, E.A.P., & Essink-Bot, M.L. (2009). Ethnic differences in considerations whether or not to participate in prenatal screening for Down Syndrome. *Prenatal Diagnosis*, 29, 1262-1269.
- French, B.N., Kurczynski, T.W., Weaver, M.T., & Pituch, M.J. (1992). Evaluation of the Health Belief Model and decision making regarding amniocentesis in women of advanced maternal age. *Health Education Quarterly*, 19(2), 177-186.
- Fuchs KM, Peipert JF. First trimester Down syndrome screening: public health implications. *Semin Perinatol*. 2005;29(4):267-71.
- Fuller, C.A. & Gallagher, R. (1999). Perceived benefits and barriers of prenatal care in low income women. *Journal of the American Academy of Nurse Practitioners*, 11(12), 527-532.
- Furr, L.A. & Seger, R.E. (1998). Psychosocial predictors of interest in prenatal genetic screening. *Psychological Reports*, 82, 235-244.
- Furr, L.A. & Seger, R.E. (1998). Psychosocial predictors of interest in prenatal genetic screening. *Psychological Reports*, 82, 235-244.
- Futch, T., Spinosa, J., Bhatt, S., de Feo, E., Rava, R.P., & Sehnert, A.J. (2013). Initial clinical laboratory experience in noninvasive prenatal testing for fetal aneuploidy from maternal plasma DNA samples. *Prenatal Diagnosis*, 33(6), 569-74.
- Garber K.B., Visootsak J., & Warren S.T. (2008). Fragile X Syndrome. *European Journal of Human Genetics*, 16, 666-672.
- Garcia, E., Timmermans, D.R.M., & van Leeuwen, E. (2008). The impact of ethical beliefs on decisions about prenatal screening tests: searching for justification. *Social Science & Medicine*, 66, 753-764.
- Garcia, J., Bicker, L., Henderson, J., Martin, M., Mugford, M., Nielson, J., & Roberts, T. (2002). Women's views of pregnancy ultrasound: A systematic review. *Birth*, 29(4), 225-250.
- Geipel, A., Berg, C., Katalinic, A., Ludwig, M., Germer, U., Diedrich, K., & Gembruch, U. (2003). Different preferences for prenatal diagnosis in pregnancies following assisted reproduction versus spontaneous conception. *Reproductive BioMedicine Online*, 8(1), 119-124.

General Medical Council (2009). *Good Medical Practice*. London: General Medical Council. Available at: www.gmc-uk.org/Static/documents/content/GMP_0910.pdf (accessed on 10 July 2011).

Georgsson, S., Sahlin, E., Iwarsson, M., Nordenkjold, M., Gustavsson, P., & Iwarsson, E. (2016). Knowledge and attitudes regarding non-invasive prenatal testing (NIPT) and preferences for risk information among high school students in Sweden. *Journal of Genetic Counseling*, doi: 10.1007/s10897-016-9997-y.

Gerber, B.S. & Eiser, A.R. (2001). The patient-physician relationship in the internet age: future prospects and the research agenda. *J Med Internet Res*, 3(2), e15.

Gil, M. M., Akolekar, R., Quezada, M. S., Bregant, B., & Nicolaides, K. H. (2014). Analysis of cell-free DNA in maternal blood in screening for aneuploidies: meta-analysis. *Fetal diagnosis and therapy*, 35(3), 156-173.

Gil, M. M., Giunta, G., Macalli, E. A., Poon, L. C., & Nicolaides, K. H. (2015). UK NHS pilot study on cell-free DNA testing in screening for fetal trisomies: factors affecting uptake. *Ultrasound in Obstetrics & Gynecology*, 45(1), 67-73.

Gil, M.M., Quezada, M.S., Revello, R., Akolekar, R., & Nicolaides, K. (2015). Analysis of cell-free DNA in maternal blood in screening for fetal aneuploidies: updated meta-analysis. *Ultrasound ObstetGynecol*, 45, 249-266.

Gil, M.M., Giunta, G., Macalli, E.A., Poon, L.C., & Nicolaides, K.H. (2015). UK NHS pilot study on cell-free DNA testing in screening for fetal trisomies: factors affecting uptake. *Ultrasound ObstetGynecol*, 45, 67-73.

Gill, V., Lavin, J., & Sim, M. (2010). Managing sickle cell disease. *Nursing made incredibly easy*, 8(6), 24-32.

Gillick, M.R. (2007). The technological imperative and the battle for the hearts of America. *Perspectives in Biology and Medicine*, 50, 276–294.

Gottfreðsdóttir, H., Björnsdóttir, K., & Sandall, J. (2009). How do prospective parents who decline prenatal screening account for their decision? A qualitative study. *Soc.Sci.Med.*, 69(2), 274-277.

Gravetter, F., & Wallnau, L. (2014). *Essentials of statistics for the behavioral sciences (8th ed.)*. Belmont, CA: Wadsworth.

Green J & Statham, H. (1996). Psychosocial aspects of prenatal screening and diagnosis. In: Marteau, T., Richards, M. (eds). *The Troubled Helix: Social and Psychological Implications of the New Human Genetics*. New York: Cambridge University Press, 140–163.

Green, J. & Thorogood, N. (2009). *Qualitative methods for health research* (2nd ed.). Thousand Oaks, CA: Sage.

Green, J.M., Hewison, J., Bekker, H.L., Bryant, L.D., & Cuckle, H.S. (2004). Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. *Health Technol Assess*, 8, 1-109.

Green, J.M., Snowden, C., & Statham, H. (1993). Pregnant women's attitudes to abortion and prenatal screening. *Journal of reproductive and infant psychology*, 11(1), 31-39.

Habing, B. (2003). *Exploratory Factor Analysis*. Website: <http://www.stat.sc.edu/~habing/courses/530EFA.pdf> (downloaded 20 November 2013).

Haga, S.B., Barry, W.T., Mills, R., Ginsburg, G.S., Svetkey, L., Sullivan, J., & Willard, H.F. (2013). Public knowledge of and attitudes toward genetics and genetic testing. *Genetic testing and molecular biomarkers*, 17(4), 327-335.

Hair, J.F. Jr., Anderson, R.E., Tatham, R.L., & Black, W.C. (1998). *Multivariate Data Analysis*, (5th Edition). Upper Saddle River, NJ: Prentice Hall.

Hallowell, N., Statham, H., Murton, F., Green, J., & Richards, M. (1997). 'Talking about chance': the presentation of risk information during genetic counseling for breast and ovarian cancer. *J Gen Counseling*, 6, 269-285.

Harris, R.A., Nease, R.F., & Kuppermann, M. (2004). Cost utility of prenatal diagnosis and the risk-based threshold. *The Lancet*, 363, 276-282.

Hart, A., Henwood, F., & Wyatt, S. (2004). The role of the internet in patient-practitioner relationships: findings from a qualitative research study. *J Med Internet Res*, 6(3), e36.

Haslam, C. & Lawrence, W. (2004). Health-related behavior and beliefs of pregnant smokers. *Health Psychology*, 23, 486-491.

Haslam, C., Lawrence, W. & Haefeli, K. (2003). Intention to breastfeed and other important health-related behaviour and beliefs during pregnancy. *Family Practice*, 20, 1-15.

Hedrick, J. (2005). The Lived Experience of Pregnancy While Carrying a Child With a Known, Nonlethal Congenital Abnormality. *Journal of Obstetric, Gynecologic, & Neonatal Nursing*, 34, 732–740.

Heinze, G. (2006). A comparative investigation of methods for logistic regression with separated or nearly separated data. *Statistics in Medicine*, 25, 4216-4226.

Henneman, L., Bramsen, I., van der Ploeg, H.M., Ader, H.J., van der Horst, H.E., Gille, J.J.P., & ten Kate, L.P. (2001). Participation in preconceptional carrier couple screening: characteristics, attitudes, and knowledge of both partners. *J Med Genet*, 38, 695-703.

Henneman, L., Timmermans, D.R.M., & Van derWal, G. (2004). Public experiences, knowledge and expectations about medical genetics and the use of genetic information. *Community Genet*, 7, 33-43.

Hertling-Schaal E., Perrotin F., De Poncheville L., Lansac J., & Body G. (2001). Maternal anxiety related to prenatal screening and invasive testing: detection and management. *Gynecology Obstetrique & Fertilité*, 29(6), 440-446.

Heyman B., Lewando Hundt G., Sandall J., Spencer K., Williams C., Grellier R., & Pitson L. (2006). On being at higher risk: A qualitative study of prenatal screening for chromosomal anomalies. *Social Science & Medicine*, 62, 2360-72.

Heyman, B., Hundt, G., Sandall, J., Spencer, K., Williams, C., Grellier, R., & Pitson, L. (2006). On being at higher risk: A qualitative study of prenatal screening for chromosomal anomalies. *Social Science and Medicine*, 62, 2360-2372.

Hill, M., Fisher, J., Chitty, L.S., & Morris, S. (2012). Women's and health professionals' preferences for prenatal tests for Down Syndrome: a discrete choice experiment to contrast noninvasive prenatal diagnosis with current invasive tests. *Genetics in Medicine*, 14(11), 905-913.

Hosseini S.M. (2007). Maternal anxiety during pregnancy: its relations to birth outcomes and to offspring depression during late childhood and adolescence. *Dissertation Abstracts International: Section B: The Sciences and Engineering*, 68(1-B), 202.

Howson C.P. & Modell B. (2008). *Controlling birth defects: reducing the hidden toll of dying and disabled children in low-income countries* (Disease Control Priorities Project). Retrieved on June 1st 2012 from www.dcp2.org

Huizink, A.C., Mulder, E.J.H., Robles de Medina, P.G.R., & Visser, G.H.A., 2004. Is pregnancy anxiety a distinctive syndrome? *Early Human Development*, 79(2), 81-91.

Hunt L.M., De Voogd K.B., & Castaneda H. (2005). The routine and the traumatic in prenatal genetic diagnosis: does clinical information inform patient decision-making? *Patient education and counselling*, 56, 302-312.

- Ilgin-Ruhi, H., Yurur-Kutlay, N., Tukun, A., & Bokesoy, I. (2005). The role of genetic counseling on decisions of pregnant women aged 35 years or over regarding amniocentesis in Turkey. *European Journal of Medical Genetics*, 48(1), 13-19.
- Jallinoja, P. & Aro, A.R. (2000). Does knowledge make a difference? The association between knowledge about genes and attitudes towards gene tests. *Journal of Health Communication*, 5, 29-39.
- Jha, P., Kumar, R., Vasa, P., Dhingra, N., Thiruchelvam, D., & Moineddin, R. (2006). Low male-to-female sex ratio of children born in India: national survey of 1· 1 million households. *The Lancet*, 367(9506), 211-218.
- Johanson, R., Newburn, M., & MacFarlane, A. (2002). Has the Medicalisation of Childbirth Gone Too Far? *BMJ: British Medical Journal*. 324(7342), 892-895.
- Jonsdottir, O.V. (2012). Medicalisation of Childbirth in Western Society: Can Women Resist the Medicalisation of Childbirth?
- Kaiser, A.S., Ferris, L.E., Katz, R., Pastuszak, A., Llewellyn-Thomas, H., Johnson, J.A., & Shaw, B.F. (2004). Psychological responses to prenatal NTS counseling and the uptake of invasive testing in women of advanced maternal age. *Patient Education and Counseling*, 54, 45-53.
- Kaiser, H. F. (1960). The application of electronic computers to factor analysis. *Educational and Psychological Measurement*, 20, 141-151.
- Kaposy, C. (2013). A disability critique of the new prenatal test for Down Syndrome. *Kennedy Institute of Ethics Journal*, 23, 299-324.
- Karasahin, E., Gezgin, K., & Alanbay, I. (2008). Expectation versus reality: A device to illustrate anticipated and perceived pain from amniocentesis. *International Journal of Gynecology and Obstetrics*, 101, 295-303.
- Karasahin, E., Gungor, S., Goktolga, U., Keskin, U., Gesgin, K., & Baser, I. (2008). Anticipated and perceived pain from mid-trimester amniocentesis. *International Journal of Gynecology and Obstetrics*, 101, 290-294.
- Kelly, S.E. & Farrimond, H.R. (2012) Non-invasive prenatal genetic testing: A study of public attitudes. *Public Health Genomics*, 15 (2), 73-81.
- Kenen, R., Smith, A.C.M., Watkins, C., & Zuber-Pittore, C. (2000). To use or not to use: male partners' perspectives on decision making about prenatal diagnosis. *Journal of Genetic Counseling*, 9(1), 33-45.

- Kenen, R.H. & Smith, A.C.M. (1995). Genetic counseling for the next 25 years: models for the future, *Journal of Genetic Counseling*, 4(2), 115–124.
- Kennerknecht, I., Baur-Aubele, S., Grab, D., & Terinde, R. (1992). First trimester amniocentesis between the seventh and thirteenth weeks: evaluation of the earliest possible genetic diagnosis. *Prenatal Diagnosis*, 12(7), 595-601.
- Kessler, S. (1997). Psychological aspects of genetic counseling: nondirectiveness revisited. *Am J Med Genet*, 72, 164–171.
- King, G., & Zeng, L. (2001). Logistic regression in rare events data. *Political analysis*, 9(2), 137-163.
- King, J.S. (2012). And genetic testing for all...The coming revolution in non-invasive prenatal genetic testing. *Rutgers Law Journal*, 42, 599-658.
- Kirkham, C., Harris, S., & Grzybowski, S. (2005). Evidence-based prenatal care: Part I. General prenatal care and counselling issues. *American Family Physician*, 71(7), 1307-1316.
- Knight, G.J., Palomaki, G.E., Neveux, L.M., Smith, D.E., Kloza, E.M., Pulkkinen, A.J., Williams, J., & Haddow, J.E. (2005). Integrated serum screening for Down Syndrome in primary obstetric practice. *Prenatal Diagnosis*, 25(12), 1162-1167.
- Kowalcek, I., Muhlhoff, A., Bachmann, S., Gembruch, U. (2002). Depressive reactions and stress related to prenatal medicine procedures. *Ultrasound Obstet Gynecol*, 19, 18–23.
- Kupperman, M., Feeny, D., Gates, E., Posner, S.F., Blumberg, B., & Washington, A.E. (1999). Preferences of women facing a prenatal diagnostic choice: long-term outcomes matter most. *Prenatal Diagnosis*, 19, 711-716.
- Labs, S.M., & Wurtele, S. K. (1986). Fetal Health Locus of Control Scale: Development and validation. *Journal of Consulting and Clinical Psychology*, 54, 814-819.
- Labs, S.M., & Wurtele, S. K. (1986). Fetal Health Locus of Control Scale: Development and validation. *Journal of Consulting and Clinical Psychology*, 54, 814-819.
- Lagan, B.M., Sinclair, M., & Kernohan, W.G. (2010). Internet use in pregnancy informs women's decision making: a web-based survey. *Birth*, 37(2), 106-115.
- Lakovschek, I. C., Streubel, B., & Ulm, B. (2011). Natural outcome of trisomy 13, trisomy 18, and triploidy after prenatal diagnosis. *Am. J. Med. Genet.*, 155, 2626–2633.

Lalor, J.G. & Devane, D. (2007). Information, knowledge and expectations of the routine ultrasound scan. *Midwifery*, 23, 13-22.

Larion, S., Warsof, S.L., Romary, L., Mlynarczyk, M., Peleg, D., & Abuhamad, A.Z. (2014). Uptake of noninvasive prenatal testing at a large academic referral center. *Am J Obstet Gynecol*, 211(6), 651-658.

Lee, A.M., Lam, S.K., Lau, S.M.S.M., Chong, C.S.Y., & Fong, D.Y.T. (2007). Prevalence, course, and risk factors for antenatal anxiety and depression. *Obstet Gynecol*, 110, 1102-1112.

Legare, F., St-Jacques, S., Gagnon, S., Njoya, M., Brisson, M., Fremont, P., Rousseau, F. (2011). Prenatal screening for Down Syndrome: a survey of willingness in women and family physicians to engage in shared decision-making. *Prenatal Diagnosis*, 31, 319-326.

Lesser, Y. & Rabinowitz, J. (2001). Elective amniocentesis in low-risk pregnancies: Decision making in the era of information and uncertainty. *American Journal of Public Health*, 91 (4), 639-641.

Lewis, C., Choudhury, M., & Chitty, L.S. (2014). 'Hope for safe prenatal gene tests'. A content analysis of how UK press media are reporting advances in non-invasive prenatal testing. *Prenatal Diagnosis*, 34, 1-8.

Lewis, C., Cullinane, F.N., Bishop, A.J., Chitty, L.S., Marteau, T.M., & Halliday, J.L. (2006). A comparison of Australian and UK obstetricians' and midwives' preferences for screening tests for Down syndrome. *Prenat Diagn*, 26, 60-66.

Lewis, C., Hill, M., & Chitty, L.S. (2016). A qualitative study looking at informed choice in the context of non-invasive prenatal testing for aneuploidy. *Prenatal Diagnosis*, 36(9), 875-881.

Lewis, C., Hill, M., & Chitty, L.S. (2016). Women's experiences and preferences for service delivery of NIPT for aneuploidy in a public health setting: A mixed methods study. *PLOS One*, 11(4), <http://doi.org/10.1371/journal.pone.0153147>

Lewis, C., Hill, M., Silcock, C., Daley, R., & Chitty, L.S. (2014). Non-invasive prenatal testing for trisomy 21: a cross-sectional survey of service users' views and likely uptake. *BJOG: An International Journal of Obstetrics and Gynaecology*, 121, 582-594.

Lewis, C., Silcock, C., & Chitty, L.S. (2013). Non-Invasive Prenatal Testing for Down's Syndrome: Pregnant Women's Views and Likely Uptake. *Public Health Genomics*, 16, 223-232.

Lippman, A. (1999). Embodied knowledge and making sense of prenatal diagnosis. *Journal of Genetic Counseling*, 8(5), 255-274.

Lo, Y.M., Corbetta, N., Chamberlain, P.F., Rai, V., Sargent, I.L., Redman, C.W., & Wainscoat, J.S. (1997). Presence of fetal DNA in maternal plasma and serum. *Lancet*, 350, 485–487.

Locock, L. & Alexander, J. (2006). 'Just a bystander'? Men's place in the process of fetal screening and diagnosis. *SocSci Med*, 62, 1349–59.

Locock, L., Field, K., McPherson, A., & Boyd, P. (2008). Women's accounts of the physical sensation of chorionic villus sampling and amniocentesis: expectations and experience. *Midwifery*, doi: 10.1016/j.midw.2008.02.002

Lou, S., Mikkelsen, L., Hvidman, L., Petersen, O.B., & Nielsen, C.P. (2015). Does screening for Down's syndrome cause anxiety in pregnant women? A systematic review. *Acta Obstet Gynecol Scand*, 94, 15–27.

Lowe, P., Powell, J., Griffiths, F., Thorogood, M., & Locock, L. (in press). "Making it all normal": The role of the internet in problematic pregnancy. UNPUBLISHED

Lumley, M.A., Zamerowski, S.T., Jackson, L., Dukes, K., & Sullivan, L. (2006). Psychosocial correlates of pregnant women's attitudes toward prenatal maternal serum screening and invasive diagnostic testing; beyond traditional risk status. *Genetic Testing*, 10(2), 131-138.

Lutgendorf, M.A., Stoll, K.A., Kmutzen, D.M., & Foglia, L.M. (2014). Non-invasive prenatal testing limitations and unanswered questions. *Genetics in Medicine*, 16(4), 281-285.

Markens, S., Browner, C.H., & Mabel, P. (2010). Interrogating the dynamics between power, knowledge, and pregnant bodies in amniocentesis decision making. *Sociology of Health & Illness*, 32(1), 37-56.

Markens, S., Browner, C.H., & Preloran, H.M. (2003). "I'm not the one they're sticking the needle into": Latino couples, fetal diagnosis, and the discourse reproductive rights. *Gender & Society*, 17, 462-481.

Markens, S., Browner, C.H., & Press, N. (1999). 'Because of the risks': how US pregnant women account for refusing prenatal screening. *Social Science and Medicine*, 49, 359-369.

Marteau, T.M. (1990). Attitudes to doctors and medicine: the preliminary development of a new scale. *Psychology and Health*, 4, 351-356.

Marteau, T.M., Dormandy, E., & Michie, S. (2001). A measure of informed choice. *Health Expectations*, 4, 99-108.

Marteau, T.M., Johnston, M., Kidd, J., Michie S., & Cook, R. (1992). Psychological models in predicting uptake of prenatal screening. *Psychology and Health*, 6, 13-22.

Marteau, T.M., Johnston, M., Plenicar, M., Shaw, R.W., & Slack, J. (1988). Development of a self-administered questionnaire to measure women's knowledge of prenatal screening and diagnostic tests. *Journal of Psychosomatic Research*, 32 (4/5), 403-408.

Marteau, T.M., Johnston, M., Shaw, R.W., Michie, S., Kidd, J., & New, M. (1989). The impact of prenatal screening and diagnostic testing upon the cognitions, emotions and behaviour of pregnant women. *Journal of Psychosomatic Research*, 33(1), 7-16.

Marteau, T.M., Kidd, J., Cook, R., Michie, S., Johnston, M., & Slack, J. (1991). Perceived risk not actual risk predicts uptake of amniocentesis. *British Journal of Obstetrics and Gynecology*, 98, 282-286.

Marteau, T.M., Kidd, J., Cook, R., Michie, S., Johnston, M., Slack, J., & Shaw, W. (1992). Psychological effects of having amniocentesis: are these due to the procedure, the risk or the behavior? *Journal of psychosomatic research*, 36 (4), 395-402.

Marteau, T.M., Kidd, J., Cook, R., Michie, S., Johnston, M., Slack, J. & Shaw, R. W. (1991), Perceived risk not actual risk predicts uptake of amniocentesis. *BJOG: An International Journal of Obstetrics & Gynaecology*, 98, 282–286.

Marteau, T.M., Saidi, G., Goodburn, S., Lawton, J., Michie, S., & Bobrow, M. (2000). Numbers or words? A randomised control trial of presenting screen negative results to pregnant women. *Prenatal Diagnosis*, 20, 714-718.

McCoyd, J.L.M. (2010). Authoritative knowledge, the technological imperative and women's responses to prenatal diagnostic technologies. *Cult Med Psychiatry*, 34, 590-614.

McMullan, M. (2006). Patients using the internet to obtain health information: How this affects the patient-health professional relationship. *Patient Education and Counseling*, 63, 24-28.

Menezes, M., Meagher, S., & Da Silva Costa, F. (2013). Ethical considerations when offering non-invasive prenatal testing. *Rev Bras Gynecol Obstet*. 35(5),195-198.

Mercer, C.H., Tanton, C., Prah, P., Erens, B., Sonnenberg, P., Clifton, S., Macdowall, W., Lewis, R., Field, N., Datta, J., Copas, A.J., Phelps, A., Wellings, K., & Johnson, A.M. (2013). Changes in sexual attitudes and lifestyles in Britain through the life course and over time: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). *Lancet*, 382, 1781-1794.

- Mercer, M.B., Agatisa, P.K., & Farrell, R.M. (2014). What patients are reading about noninvasive prenatal testing: an evaluation of internet content and implications for patient-centered care. *Prenatal Diagnosis*, 34, 986-993.
- Michie, S., Bron, F., Bobrow, M., & Marteau, T.M. (1997). Nondirectiveness in genetic counseling: an empirical study. *Am J Hum Genet*, 60, 40–47.
- Michie, S., Dormandy, E., French, D.P., & Marteau, T.M. (2004). Using the theory of planned behaviour to predict screening uptake in two contexts. *Psychol Health*, 19, 705–718.
- Michie, S., Dormandy, E., Marteau, T. M. (2002). The multi-dimensional measure of informed choice: a validation study. *Patient Education and Counseling*, 48, 87-91.
- Michie, S., Drake, H., Bobrow, M., & Marteau, T. (1995). A comparison of public and professionals' attitudes towards genetic developments. *Public Understanding of Science*, 4, 243-253.
- Milic, B., Babic, I., Ristic, S., Vranekovic, J., Brumini, G., & Kapovic, M. (2008). Pregnant women's attitudes toward amniocentesis before receiving Down Syndrome screening results. *Women's Health Issues*, 18, 79-84.
- Mischler E. (1984). *The discourse of medicine: dialectics of medical interviews*. Norwood, NJ: Ablex Publishing Corporation.
- Mishler, E. (1984). *The discourse of medicine: dialectics of medical interviews*. Norwood, NJ: Ablex Publishing Corporation.
- Morahan-Martin, J.M. (2004). How internet users find, evaluate and use online health information: a cross-cultural review. *Cyberpsychology & Behavior*, 7(5), 497-510.
- Morren, M., Rijken, M., Baanders, A.N., & Bensing, J. (2007). Perceived genetic knowledge, attitudes towards genetic testing, and the relationship between these among patients with a chronic disease. *Patient Education and Counselling*, 65, 197-204.
- Morris, S., Karlsen, S., Chung, N., Hill, M., & Chitty, L.S. (2014). Model-based analysis of costs and outcomes of non-invasive prenatal testing for Down's syndrome using cell free fetal DNA in the UK National Health Service. *PloSone*, 9(4), e93559.
- Moumjid, N., Gafni, A., Bremond, A., & Carrere, M.O. (2007). Decision making in the medical encounter: Are we all talking about the same thing? *Medical Decision Making*, 27, 539-548.

Moyer, A., Brown, B., Gates, E., Daniels, M., Brown, H.D., & Kuppermann, M. (1999). Decisions about prenatal testing for chromosomal disorders: perceptions of a diverse group of pregnant women. *Journal of Women's Health & Gender-based Medicine*, 8(4), 521-531.

Mueller, V.M., Huang, T., Summers, A.M., & Winsor, H.M. (2005). The influence of risk estimates obtained from maternal serum screening on amniocentesis rates. *Prenatal Diagnosis*, 25, 1253-1257.

Murdoch, B., Ravitsky, V., Ogbogu, U., Ali-Khan, S., Bertier, G., Birko, S., Bubela, T., De Beer, J., Dupras, C., Ellis, M., Moreno, P.G., Joly, Y., Kamenova, K., Master, Z., Marcon, A., Paulden, M., Rousseau, F., & Caulfield, T. (2016). Non-invasive prenatal testing and the unveiling of an impaired translation process. *JOCG*, <http://dx.doi.org/10.1016/j.jogc.2016.09.004>

Murray, E., Lo, B., Pollack, L., Donelan, K., Catania, J., Zapert, L.K., & Turner, R. (2003). The impact of health information on the internet on health care and the physician-patient relationship: National US Survey among 1.050 US Physicians. *J Med Internet Res*, 5(3), e17.

National Institute for Health and Clinical Excellence [NICE] (2008). *NICE clinical guideline 62. Antenatal care: Routine care for the healthy pregnant woman*.

National Screening Committee (NSC, 2015). *Screening tests for you and your baby*. Available at <http://www.screening.nhs.uk/annbpublications>

NCHPEG (2012). *Non-invasive prenatal testing (NIPT) factsheet*. Retrieved December 1, 2016 from http://www.nchpeg.org/index.php?option=com_content&view=article&id=384&Itemid=255.

Ng, C.C.M., Lai, F.M., Yeo, G.S.H. (2004). Assessment of maternal anxiety levels before and after amniocentesis. *Singapore Med J*, 45(8), 370-4.

NHS FASP (2010). *Fetal Anomaly Screening Programme*.

NICE (2008). *Antenatal Care: Routine care for the healthy pregnant woman*. NICE Clinical Guidelines, No.62. National Collaborating Centre for Women's and Children's Health (UK). London: RCOG Press.

Nicolaides, K.H. (2004). Nuchal translucency and other first-trimester sonographic markers of chromosomal abnormalities. *Am J Obstet Gynecol*, 191, 45-67.

Nicolaides, K.H. (2011). Screening for fetal aneuploidies at 11 to 13 weeks. *Prenat Diagn*, 31, 7-15.

Nicolaides, K.H., Chervenak, F.A., McCullough, L.B., Avgidou, K., & Papageorghiou, A. (2005). Evidence-based obstetric ethics and informed decision-making by pregnant women about

invasive diagnosis after first-trimester assessment of risk for trisomy 21. *American Journal of Obstetrics and Gynecology*, 193, 322-326.

Nicolaides, K.H., Syngelaki, A., Ashoor, G., Birdir, C., & Touzet, G. (2012). Non-invasive prenatal testing for fetal trisomies in a routinely screened first-trimester population. *Am J Obstet Gynecol*, 207, 374-380.

Nicolaides, K.H., Syngelaki, A., Gil, M., Atanasova, V., & Markova D. (2013). Validation of targeted sequencing of single-nucleotide polymorphisms for non-invasive prenatal detection of aneuploidy of chromosomes 13, 18, 21, X, and Y. *Prenat Diagn*, 33, 575–579.

Nicolaides, K.H., Syngelaki, A., Poon, L.C., Gil, M.M., & Wright, D. (2014). First-trimester contingent screening for trisomies 21, 18 and 13 by biomarkers and maternal blood cell-free DNA testing. *Fetal Diagn Ther*, 35, 185–192.

Norton, M.E., Brar, H., & Weiss, J. (2012). "Non-Invasive Chromosomal Evaluation (NICE) study: results of a multicentre prospective cohort study for detection of fetal trisomy 21 and trisomy 18," *American Journal of Obstetrics & Gynecology*, vol. 207, no. 2, pp. 137.e1–137.e8.

Norton, M.E., Brar, H., & Weiss, J. (2012). Noninvasive chromosomal evaluation (NICE) study: results of a multicenter prospective cohort study for detection of fetal trisomy 21 and trisomy 18. *Am J Obstet Gynecol*, 207, 137-145.

Norwitz, E.R. & Levy, B. (2013). Non-invasive prenatal testing: the future is now. *Reviews in Obstetrics & Gynecology*, 6(2), 48-62.

NSC – National Screening Committee (2015). Screening tests for you and your baby. Available at www.screening.nhs.uk

O'Connor, A. M., Bennett, C. L., Stacey, D., Barry, M., Col, N. F., & Eden, K. B., (2009). Decision aids for people facing health treatment or screening decisions. *Cochrane Database Systematic Reviews*, (3), CD001431.

O'Connor, A.M. & O'Brien-Pallas, L.L. (1989). *Decisional conflict*. In: McFarlane, G.K. & McFarlane, E.A. (eds), *Nursing Diagnosis and Intervention*. Toronto: Mosby, pp.486-496.

O'Connor, A.M., Bennett, C.L., Stacey, D., Barry, M., Col, N.F., Eden, K.B., Entwistle, V.A., Fiset, V., Holmes-Rovner, M., Khangura, S., Llewellyn-Thomas, H., & Rovner, D. (2009). Decision aids for people facing health treatment or screening decisions (Review). *Cochrane Database of Systematic Reviews*, Issue 3. Art, No: CD001431. DOI: 10.1002/14651858.cd001431.pub2.

Oakley, A. (1984). *The captured womb*. Oxford: Blackwell.

Office for National Statistics (2013). Detailed characteristics for England and Wales, 2011. Available at: http://www.ons.gov.uk/ons/dcp171778_310514.pdf

Office for National Statistics (2013). Live births in England and Wales by characteristics of Mother 1, 2013. Available at: <http://www.ons.gov.uk/ons/rel/vsob1/characteristics-of-Mother-1--england-and-wales/2013/stb-characteristics-of-mother-1--2013.html>

Ohman, S.G., Saltvedt, S., Grunewald, C., & Waldenstrom, U. (2004). Does fetal screening affect women's worries about the health of their baby? *Acta Obstet Gynecol Scand*, 83, 634-640.

Ohman, S.G., Saltvedt, S., Waldenstrom, U., Grunewald, C., & Olin-Lauritzen, S. (2006). Pregnant women's responses to information about an increased risk of carrying a baby with Down Syndrome.

Palomaki, G.E., Deciu, C., Kloza, E.M., Lambert-Messerlian, G.M., Haddow, J.E., Neveux, L.M., Ehrich, M., van den Boom D., Bombard, A.T., Grody, W.W., Nelson, S.F., & Canick, J.A.(2012). DNA sequencing of maternal plasma reliably identifies trisomy 18 and trisomy 13 as well as Down syndrome: an international collaborative study. *Genet Med*, 14, 296–305.

Palomaki, G.E. (2011). Prenatal identification of trisomy 18 (Edwards syndrome). Retrieved 09/01/2012 from <http://qmro.qmul.ac.uk/jspui/handle/123456789/1317>

Panomai, N., Sanchaisuriya, K., Yamsri, S., Sanchaisuriya, P., Fucharoen, G., Fucharoen, S., & Schelp, F.P. (2010). Thalassemia and iron deficiency in a group of northeast Thai school children: relationship to the occurrence of anemia. *European Journal of Pediatrics*, 169(11), 1317-1322.

Pearson, K. (1901). On lines and planes of closest fit to systems of points in space. *Philosophical Magazine* 2, 559-572.

People Science & Policy. Choosing the Future: Genetics and Reproductive Decision-Making Analysis of responses to the consultation Final report prepared for The Human Genetics Commission, May, 2005.

Perneger, T.V. (1998). What's wrong with Bonferroni adjustments. *BMJ*, 316, 1236-1238.

Pesso R., Berkenstadt M., Cuckle H., Gak E., Peleg L., Frydman M., & Barkai G. (2000). Screening for fragile X syndrome in women of reproductive age. *Prenatal Diagnosis*, 20, 611-614.

Phipps, S. & Zinn, A.B. (1986). Psychological response to amniocentesis: II. Moodstate and adaptation to pregnancy [abstract]. *Am J Med Genet*, 25(1),131–42.

- Pighin, S., Bonnefon, J.F., & Savadori, L. (2011). Overcoming number numbness in prenatal risk communication. *Prenatal Diagnosis*, 31, 809-813.
- Pitukijronnakorn, S., Promsonti, P., Panburana, P., Rangsiarakarn, R., & Chittacharoen, A. (2008). Prenatal Ultrasonographic Findings in "Trisomy 13". *Journal of the Medical Association of Thailand*, 91(11), 1651-1655.
- Posner, S.F., Learman, L.A., Gates, E.A, Washington, A.E., & Kuppermann, M. (2004). Development of an attitudes measure for prenatal screening in diverse populations. *Social Indicators Research*, 65, 187-206.
- Powell, J.A., Lowe, P., Griffiths, F.E., & Thorogood, M. (2005). A critical analysis of the literature on the internet and consumer health information. *Journal of telemedicine and telecare*, 11(suppl 1), 41-43.
- Prajapati, B., Dunne, M., & Armstrong, R. (2010). Sample size estimation and statistical power analyses. *Optometry Today*, 16(07), 10-18.
- Preece, M.A. & Green, A. (2002). Pregnancy and inherited metabolic disorders: maternal and fetal complications. *Annals of Clinical Biochemistry*, 39(5), 444-455.
- Press, N. & Browner, C.H. (1997). Why women say yes to prenatal diagnosis. *Social Science & Medicine*, 45(7), 979-989.
- Quine, L. & Rubin, R. (1997). Attitude, subjective norm and perceived behavioural control as predictors of women's intentions to take hormone replacement therapy. *British Journal of Health Psychology*, 2, 199-216.
- Rado, S.N., Kosec, V., & Gall, V. (2013). The psychological effects of prenatal diagnostic procedures: maternal anxiety before and after invasive and non-invasive procedures. *Prenatal Diagnosis*, 33, 1194-1200.
- Rao, M. (1997). An exploration of the predictability of drinking behavior of pregnant women using selected dimensions of the health belief model and the fetal health Locus of Control scale. *Dissertation Abstracts International: Section B: The Sciences and Engineering*, 57, 7218.
- Rapp, R. (1999). Testing women, testing the fetus. New York: Routledge.
- Ravitsky V. Non-invasive prenatal diagnosis: an ethical imperative. *Nat Rev Genet* 2009; 10:733–733.
- Raymond F.L., Whittaker J., Jenkins L., Lench N., & Chitty L.S. (2010). Molecular prenatal diagnosis: the impact of modern technologies. *Prenatal Diagnosis*, 30, 674-681.

RCOG (2014). Non-invasive prenatal testing for chromosomal abnormality using maternal plasma DNA. Scientific Impact Paper, No15.

Rees, D.C., Williams, T.N., & Gladwin, M.T. (2010). Sickle-cell disease. *Lancet*, 376, 2018-2031.

Reis F.M., D'Antona D. & Petraglia F. (2002). Predictive Value of Hormone Measurements in Maternal and Fetal Complications of Pregnancy. *Endocrine Reviews*, 23(2), 230–257.

Remennick, L. (2006). The quest for the perfect baby: why do Israeli women seek prenatal genetic testing? *Sociology of Health & Illness*, 28(1), 21-53.

Rempel, G.R., Gender, L.M., Lynam, M.J., Sandor, G.G., & Farquharson, D. (2004). Parents' perspectives on decision making after antenatal diagnosis of congenital heart disease. *JOGNN*, 33(1), 64-70.

Ressler, I.B., Bessett, D., Sroga, J.M., Rompola, S., Ferrari, R.M., Thomas, M.A., & Lindheim, S.R. (2014). The road to fatherhood using assisted reproduction technology: decision making processes and experiences among gay male intended parents and gestational surrogates. *Gynecol/Obstet Res Open J*, 1(1), 12-17.

Roelofsen, E.E.C., Kamerbeek, L.I., Tymstra, T., Beekhuis, J.R., & Mantingh, A. (1993). Women's opinions on the offer and use of maternal serum screening, *Prenatal Diagnosis*, 13, 741–747.

Rosen, T. & D'Alton, M.E. (2005). Down syndrome screening in the first and second trimester: what do the data show? *Semin Perinatol*, 29(6), 367-275.

Rothman, K.J. (1990). No adjustments are needed for multiple comparisons. *Epidemiology*, 1, 43-46.

Rowley, P.T., Loader, S., Sutera, C.J., Walden, M., & Kozyra, A. (1991). Prenatal screening for hemoglobinopathies. III. Applicability of the Health Belief Model. *American Journal of Human Genetics*, 48, 452-459.

Royal College of Obstetricians and Gynaecologists (2005). Amniocentesis and Chorionic Villus Sampling. London: RCOG.

Royal College of Obstetricians and Gynaecologists (2010). *Termination of pregnancy for fetal abnormality in England, Scotland, and Wales. Report of a working party*. London: RCOG.

Ruhi, H., Kutlay, N., Tukun, A., & Bokesoy, I. (2005). The role of genetic counseling on decisions of pregnant women aged 35 years or over regarding amniocentesis in Turkey. *European Journal of Medical Genetics*, 48, 13-19.

Ruxton, G. (2006). The unequal variance t-test is an underused alternative to Student's t-test and the Mann-Whitney U test. *Behavioral Ecology*, 17(4), 688-690.
<http://dx.doi.org/10.1093/beheco/ark016>

Sagi, M., Shiloh, S., & Cohen, T. (1992). Application of the Health Belief Model in a study on parents' intentions to utilize prenatal diagnosis of cleft lip and/or palate. *American Journal of Medical Genetics*, 44, 326-333.

Sahlin, E., Nordenskjold, M., Gustavsson, P., Wincent, J., Georgsson, S., & Iwarsson, E. (2016). Positive attitudes towards non-invasive prenatal testing (NIPT) in a Swedish cohort of 1,003 pregnant women. *PLoS One*, 11(5). <http://dx.doi.org/10.1371/journal.pone.0156088>

Saisto, T., Salmela-Aro, K., Nurmi, J.E., Kononen, T., & Halmesmaki, E. (2001). A randomized controlled trial of intervention in fear of childbirth. *Obstetrics and Gynecology*, 98(5), 820-826.

Santalahti, P., Aro, A.R., Hemminki, E., Helenius, H., & Ryyanen, M. (1998). On what grounds do women participate in prenatal screening? *Prenatal Diagnosis*, 18, 153-165.

Santalahti, P., Hemminki, E., Latikka, A.M., & Ryyanen, M. (1997). Women's decision making in prenatal screening. *Social Science and Medicine*, 46 (8), 1067-1076.

Sapp J.C., Hull S.C., Duffer S., Zornetzer S., Sutton E., Marteau T.M., & Biesecker B.B. (2010). Ambivalence toward undergoing invasive prenatal testing: an exploration of its origins. *Prenatal Diagnosis*, 30, 77-82.

Saucier, J.B., Johnston, D., Wicklund, C.A., Robbins-Furman, P., Hecht, J.T., & Monga, M. (2005). Racial-ethnic differences in genetic amniocentesis uptake. *Journal of Genetic Counseling*, 14(3), 189-195.

Sayres, L.C., & Cho, M.K. (2011). Cell-free fetal nucleic acid testing: a review of the technology and its applications. *Obstet Gynecol Surv*, 66(7), 431-442.

Schmitz, D., Henn, W., & Netzer, C. (2009). No risk, no objections? Ethical pitfalls of cell-free fetal DNA and RNA testing. *BMJ*, 339 165.

Schuchter K., Hafner E., Stangl G., Metzenbauer M., Hofinger D., & Philipp K. (2002). The first trimester 'combined test' for the detection of Down syndrome pregnancies in 4939 unselected pregnancies. *Prenatal Diagnosis*, 22(3), 211-215.

- Sedlmeier, P., & Gigerenzer, G. (1989). Do studies of statistical power have an effect on the power of studies?. *Psychological bulletin*, 105(2), 309.
- Sermon, K., Van Steirteghem, A., & Liebaers, I. (2004). Preimplantation genetic diagnosis. *The Lancet*, 363(9421), 1633-1641.
- Sewry C.A. (2010). Muscular dystrophies: an update on pathology and diagnosis. *Acta Neuropathologica*, 120, 343-358.
- Shavlev, D. (2003). *The Gap between Positive and Negative Pregnancy Experiences among Young Israeli Mothers*. An unpublished MA thesis. Bar Ilan University, Department of Sociology and Anthropology.
- Sheih, C., Broome, M. E., & Stump, T. (2010). Factors associated with health information-seeking in low-income pregnant women. *Women & Health*, 5, 426-442.
- Sheridan, S.L., Harris, R.P., Woolf, S.H. (2004). Shared decision-making about screening and chemoprevention: a suggested approach from the U.S. Preventive Services Task Force. *Am J Prev Med*, 26, 56–66.
- Sherman S., Pletcher B.A., & Driscoll D.A. (2005). Fragile X syndrome: diagnostic and carrier testing. *Genetics in Medicine*, 7(8), 584-587.
- Sherod C., Sebire N.J., Soares W., Snijders R.J.M., Nicolaides K.H. (1997). Prenatal diagnosis of trisomy 18 at the 10-14 week ultrasound scan, *Ultrasound in Obstetrics and Gynecology* (10), 387-390.
- Shiloh, S. (1996). Decision making in the context of genetic risk. In *The Troubled Helix: Social and Psychological Implications of the New Human Genetics*, Marteau, T.M., Richards, M. (eds). Cambridge University Press: Cambridge; 82–103.
- Shiloh, S. (2006). Genetic Counseling: Psychological Models in research and practice. *Encyclopedia of Life Sciences*, doi: 10.1002/9780470015902.a0005624
- Siegrist, M., Cousin, M.E., & Keller, C. (2008). Risk communication, prenatal screening, and prenatal diagnosis: the illusion of informed decision-making. *Journal of Risk Research*, 11(1-2), 87-97.
- Singer, E. (1991). Public attitudes toward genetic testing. *Popul Res Policy Rev*, 10(3), 235-255.
- Sjogren, B. & Uddenber, N. (1988). Attitudes towards disabled persons and the possible effects of prenatal diagnosis: An interview study among 53 women participating in prenatal diagnosis and 20 of their husbands. *J Psychosomat Obstet Gynaecol*, 6, 187–196.

Skirton, H. & Jackson, L. (2015). Factors affecting the clinical use of Non-invasive prenatal testing. *Journal of Clinical Diagnosis and Research*, 3(1), 121-122.

Smetana, J.G. (1979). Beliefs about the permissibility of abortion and their relationship to decisions regarding abortion. *Journal of population*, 2(4), 294-305.

Sommerhalder, K., Abraham, A., Zufferey, M.C., Barth, J., & Abel, T. (2009). Internet information and medical consultations: experiences from patients' and physicians' perspectives. *Patient Education and Counseling*, 77, 266-271.

Song, K., Musci, T.J., & Caughey, A.B. (2013). Clinical utility and cost of non-invasive prenatal testing with cfDNA analysis in high-risk women based on a US population. *The Journal of Maternal-Fetal & Neonatal Medicine*, 26(12), 1180-1185.

Sparbel K.J.H. & Williams J.K. (2009). Pregnancy as foreground in Cystic Fibrosis carrier testing decisions in primary care. *Genetic Testing and Molecular Biomarkers*, 13(1), 133-142.

Sparks, A.B., Struble, C.A., Wang, E.T., Song, K., and Oliphant, A. (2012). "Noninvasive prenatal detection and selective analysis of cellfreeDNA obtained frommaternal blood: evaluation for trisomy 21 and trisomy 18," *American Journal ofObstetrics&Gynecology*, vol. 206, no. 4, pp. 319.e1–319.e9.

Spencer K., Charas O., Skentou H., Liao A.W., & Nicolaides K.H. (2000). Screening for trisomy 13 by fetal nuchal translucency and maternal serum free b-cHG and PAPP-A at 10-14 weeks of gestation, *Prenatal Diagnosis* (20), 411-416.

Spies S., Schipper K., Nollet F., & Abma T.A. (2010). A patient's journey: Duchenne muscular dystrophy. *British Medical Journal*, 341, 1101-1103.

Srinivasan, A., Bianchi, D.W., Huang, H., Sehnert, A.J., &Rava, R.P. (2013).Non-invasive detection of fetal sub-chromosome abnormalities via deep sequencing of maternal plasma.*Am J Hum Genet*, 92, 167–176.

Statham, H., Green, J., & Katesios, K. (1997). Who worries that something might be wrong with the baby? A prospective study of 1072 women. *Birth*, 24.

Steinberg, M.H. (2011). Sickel Cell Disease. *Annals of Internal Medicine*, 155(5), ITC3-1 (15 pages).

Steptoe, A., & Wardle, J. (2001). Health behaviour, risk awareness and emotional wellbeing in students from Eastern Europe and Western Europe. *Social Science and Medicine*, 53, 1621-1630.

- Stevens, J. (1986). *Applied multivariate statistics for the social sciences*. Hillsdale, NJ: Lawrence Erlbaum Associates.
- Sun, J.C., Hsia, P.H., & Sheu, S.J. (2008). Women of advanced maternal age undergoing amniocentesis: a period of uncertainty. *Maternal & Neonatal Health*, 17, 2829-2837.
- Sundberg K., Bang J., Smidt-Jensen S., Brocks V., Lundsteen C., Parner J., Keiding N., and Philip J. (1997). Randomised study of risk of fetal loss related to early amniocentesis versus chorionic villus sampling. *Lancet*, 350 (9079) , pp. 697-703.
- Sutton, S. (1994). The past predicts the future: Interpreting behaviour-behaviour relationships in social psychological models of health behaviours. In D. R. Rutter & L. Quine (Eds), *Social Psychology and Health: European Perspectives*, pp. 71-88. Aldeahot: Avebury.
- Tabachnick, B.G.; Fidell, L.S. (2001). *Using Multivariate Analysis*. Boston: Allyn and Bacon.
- Tabor, A., &Alfirevic, Z. (2010). Update on procedure-related risks for prenatal diagnosis techniques. *Fetal Diagn Ther*, 27, 1–7.
- Tan, J.A., Lee, P.C., Wee, Y.C., Tan, K.L., Mahali, N.F., George, E., & Chua, K.H. (2010). High prevalence of Alpha- and Beta-Thalassemia in the Kadazandusuns in East Malaysia: challenges in providing effective health care for an indigenous group. *Journal of Biomedicine and Biotechnology*, 2010, 1-5.
- Taylor, H. & Leitman, R. (2002). Four-nation survey shows widespread but different levels of internet use for health purposes. *Health Care News*, 2(11). Available at <http://harrisinteractive.com/news/newslettershealthcare.asp>
- Taylor, I. (2000). Some patients are happy for doctors to make decisions. *British Medical Journal*, 320, 58.
- Tercanli, S., Vial, Y., & Merz, E. (2013). Non-invasive prenatal testing raises concern over screening strategies and the role of ultrasound. *Ultraschall in Med*, 34(5), 417-420.
- Tercyak, K.P., Johnson, S.B., Roberts, S.F., & Cruz, A.C. (2001). Psychological response to prenatal genetic counseling and amniocentesis. *Patient Education and Counseling*, 43, 73-84.
- Tiedje, L.B., Kingry, M.J., & Stommel, M. (1992). Patient attitudes concerning health behaviors during pregnancy: initial development of a questionnaire. *Health Education Quarterly*, 19(4), 481-493.
- Tipping, M.E. & Bishop, C.M. (1999). Mixtures of probabilistic Principal Component Analysers. *Neural Computation* 11(2), 443-482.

Trochim, W. M., & Donnelly, J. P. (2006). *The research methods knowledge base (3rd ed.)*. Cincinnati, OH: Atomic Dog.

Turrieff-Jonasson, S. (2004). *Use of prenatal testing, emotional attachment to the fetus and fetal health locus of control*. Unpublished master's thesis, University of Saskatchewan, Saskatoon.

Tversky, A. & Kahneman, D. (1981). The framing of decisions and the psychology of choice. *Science*, 211, 453 - 458.

Tymstra T. (2007). 'At least we tried everything': About binary thinking, anticipated decision regret, and the imperative character of medical technology. *Journal of Psychosomatic Obstetrics & Gynecology*, 28(3), 131.

Tymstra, T. (1989). The imperative character of technology and the meaning of "anticipated decision regret". *International Journal of Technology Assessment in Health Care*, 5, 207-213.

Tymstra, T. (1991). Prenatal diagnosis, prenatal screening, and the rise of the tentative pregnancy. *International Journal of Technology Assessment in Health Care*, 7(4), 509-516.

Ubel, P.A. (2010). Beyond costs and benefits: understanding how patients make health care decisions. *The Oncologist*, 15(suppl 1), 5-10.

Vahanian, S. A., Baraa Allaf, M., Yeh, C., Chavez, M. R., Kinzler, W. L., & Vintzileos, A. M. (2014). Patient acceptance of non-invasive testing for fetal aneuploidy via cell-free fetal DNA. *The Journal of Maternal-Fetal & Neonatal Medicine*, 27(1), 106-109.

Van den Berg, M., Timmermans, D.R.M., Kleinveld, J.H., Garcia, E., van Vugt, J.M.G., & van der Wal, G. (2005). Accepting or declining the offer of prenatal screening for congenital defects: test uptake and women's reasons. *Prenatal Diagnosis*, 25, 84-90.

Van den Berg, M., Timmermans, D.R.M., Kleinveld, J.H., van Eijk, J.T.M., Knol, D.L., van der Wal, G., & van Vugt, J.M.G. (2007). Are counsellors' attitudes influencing pregnant women's attitudes and decisions on prenatal screening? *Prenatal Diagnosis*, 27, 518-524.

Van den Berg, M., Timmermans, D.R.M., Knol, D.L., Van Eijk, J.T.M., De Smit, D.J., Van Vugt, J.M.G., & Van der Wal, G. (2008). Understanding pregnant women's decision making concerning prenatal screening. *Health Psychology*, 27(4), 430-437.

Van den Berg, M., Timmermans, D.R.M., Ten Kate, L.P., Van Vugt, J.M.G., & Van der Wal, G. (2006). Informed decision making in the context of prenatal screening. *Patient Education and Counseling*, 63, 110-117.

Van Schendel, r.v., Dondorp, w.j., Timmermans, D.R., van Hugle, e.j., DE boer, A., Pajkrt, E., Lachmeijer, A.M., & Henneman, L. (2015). NIPT-based screening for Down Syndrome and beyond: what do pregnant women think? *Prenatal Diagnosis*, 35(6), 598-604.

Van Schendel, R.V., Kater-Kuipers, A. van Vliet-Lachotzki, E.H., Dondorp, W.J., Cornel, M.C., & Henneman, L. (2016). What do parents of children with Down Syndrome think about non-invasive prenatal testing (NIPT)? *J Genet Counsel*, doi:10.1007/s10897-016-0012-4.

Vanstone, M., King, C., de Vrijer, B., & Nisker, J. (2014). Non-invasive prenatal testing: ethics and policy considerations. *Journal of Obstetrics and Gynaecology Canada*, 36(6), 515-526.

Venables, W. N. and Ripley, B. D. (2002) *Modern Applied Statistics with S*. New York: Springer (4th ed)

Vergani, P., Locatelli, A., Biffi, A., Ciriello, E., Zagarella, A., Pezzullo, J., & Ghidini, A. (2002). Factors affecting the decision regarding amniocentesis in women at genetic risk because of age 35 years or older. *Prenatal Diagnosis*, 22, 769-774.

Verweij, J., de Boer, M.A., & Oepkes, D. (2014). Non-invasive prenatal testing for trisomy 13: more harm than good? *Ultrasound Obstet Gynecol*, 44, 112-114.

Vigan, C., Vodovar, V., Goujard, J., Garel, M., Vayssiere, F., Goffinet, F. (2002). *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 104, 14-20.

Vogt, C.A. & Fesenmaier, D.R. (1998). Expanding the functional information search model. *Annals of tourism research*, 25(3), 551-578.

Vora, N.L., & O'Brien, B.M. (2014). Non-invasive prenatal testing for microdeletion syndromes and expanded trisomies: proceed with caution. *Obstet Gynecol*, 123, 1097–1099.

Wallston, K. A., Maides, S. A., & Wallston, B. S. (1976). Health-related information seeking as a function of health-related locus of control and health value. *Journal of Research in Personality*, 10, 215-222.

Wallston, K. A., Wallston, B. S., & DeVellis, R. (1978). Development of the multidimensional health locus of control (MHLC) scales. *Health Education Monographs*, 6, 160-170.

Wallston, K.A. (2005). The validity of the Multidimensional Health Locus of Control Scales. *Journal of Health Psychology*, 10, 623-631.

Wallston, K.A. & Wallston, B.S. (2005). The validity of the multidimensional Health Locus of Control Scales. *Journal of Health Psychology*, 10(4), 623-631.

- Wang, E., Batey, A., Struble, C., Musci, T., Song, K., & Oliphant, A. (2013). Gestational age and maternal weight effects on cell-free DNA in maternal plasma. *Prenatal Diagnosis*, 33, 662-666.
- Weatherall D.J. (2000). Single gene disorders of complex traits: lessons from the thalassaemias and other monogenic diseases. *BMJ*, 321(7269), 1117-1120.
- Weatherall D.J., Akinyanju O., Fucharoen S., Olivieri N. & Musgrove P. (2006). *Inherited disorders of Haemoglobin*. In: Disease control priorities in developing countries (ed. by Jamison D. et al), pp. 663-680. Oxford University and the World Bank, New York.
- Weil, J. (2003). Psychosocial genetic counseling in the post-nondirective era: a point of view. *J Genet Couns* 12, 199–211.
- Weinans, M.J.N., Huijssoon, A.M.G., Gerrits, M.C.F., Beekhuis, J.R., & Mantingh, A. (2000). How women deal with the results of serum screening for Down syndrome in the second trimester of pregnancy. *Prenatal Diagnosis*, 20, 705-708.
- Welkenhuysen, M., Evers-Kiebooms, G., & Ydewalle, G. (2001). The language of uncertainty in genetic risk communication: framing and verbal versus numerical information. *Patient Education and Counseling*, 43, 179-187.
- Wertz, D.C., & Fletcher, J.C. (1993). A critique of some feminist challenges to prenatal diagnosis. *J Womens Health*, 2, 173–188.
- WHO (2006). Joint WHO-March of Dimes meeting on the management of birth defects and haemoglobin disorders. Geneva: WHO.
- Widaman, K.F. (1993). Common factor analysis versus principal component analysis: differential bias in representing model parameters? *Multivariate Behavioral Research*, 28(3), 263-311.
- Williams C., Anderson P., & Farsides B. (2002). Is nondirectiveness possible within the context of antenatal screening and testing? *Social Science Medicine*, 54, 339-347.
- Williams, C., Alderson, P., & Farsides, B. (2002) Too Many Choices? Hospital and community staff reflect on the future of prenatal screening. *Social Science & Medicine*, 55, 743-753.
- Yagel, S. (2013). Non-invasive prenatal testing: more questions than answers. *Ultrasound Obstet Gynecol*, 42, 369–372.
- Zamerowski, S.T., Lumley, M.A., Arreola, R.A., Dukes, K., & Sullivan, L. (2001). Favourable attitudes toward testing for chromosomal abnormalities via analysis of fetal cells in maternal blood. *Genetics in Medicine*, 3(4), 301-309.

Ziefle, M. & Shaar, M.K. (2011). Gender differences in acceptance and attitudes towards an invasive medical stent. *Electronic Journal of Health Informatics*, 6(2), 13-30.

Zigmond, A. S., & Snaith, R.P. (1983). The Hospital Anxiety and Depression Scale, *Acta Psychiatrica Scandinavica*, 67, 361-370.

Zikmund-Fisher, B.J., Fagerlin, A., Keeton, K., & Ubel, P.A. (2007). Does labelling prenatal screening test results as negative or positive affect a woman's responses? *American Journal of Obstetrics & Gynecology*, 197:528.e1-528.e6. (doi: 10.1016/j.ajog.2007.03.076)

Zlotogora, J. (2002). Parental decisions to abort or continue a pregnancy with an abnormal finding after an invasive prenatal test. *Prenatal Diagnosis*, 22, 1102-1106.

6. Appendixes

6.1. Appendix 1: Original Questionnaire (pilot study)

For the following statements please cross the box that best suits you.

OFFICE USE Date: _____
ONLY Patient ID: _____

SECTION A: AMNIOCENTESIS / CVS

For the following statements, please cross the box that you think is the correct answer.

1) The purpose of amniocentesis/CVS is to test for:

- ☐ 1 Diabetes
☐ 2 Pregnancy
☐ 3 Chromosomal disorders
☐ 4 Don't know

2) The result of amniocentesis/CVS is 100% reliable.

- ☐ 1 True ☐ 2 False

3) Amniocentesis/CVS have around 1% chance of causing miscarriage.

- ☐ 1 True ☐ 2 False

4) If amniocentesis/CVS shows that the baby definitely has a chromosomal disorder, what options would a woman be offered?

- ☐ 1 Immediate treatment for the baby
☐ 2 Another type of test
☐ 3 A termination of pregnancy
☐ 4 Extra vitamins
☐ 5 None of the above
☐ 6 Not sure

SECTION B: YOU & AMNIOCENTESIS / CVS

For the following statements, please cross the box that best describes how you feel at the moment.

1) For me, having an amniocentesis/CVS would be:


- ☐ 1 Not at all beneficial
☐ 2 Less than beneficial
☐ 3 Neutral
☐ 4 Somewhat beneficial
☐ 5 Very beneficial
☐ 6 Don't know

2) For me, from a physical point of view, having amniocentesis/CVS would be:

- ☐ 1 Extremely unpleasant
☐ 2 Very unpleasant
☐ 3 Neutral
☐ 4 Somewhat pleasant
☐ 5 Not at all unpleasant
☐ 6 Don't know

3) Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not:

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree
☐ 6 Don't know

Section B continues on the next page 

[Section B continues here]

4) I believe invasive diagnostic tests, such as amniocentesis and CVS, should never be done because they go against human nature.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree
☐ 6 Don't know

5) For me, having an amniocentesis/ CVS would be:

- ☐ 1 Not at all reassuring
☐ 2 Less than reassuring
☐ 3 Neutral
☐ 4 Somewhat reassuring
☐ 5 Very reassuring
☐ 6 Don't know

6) For me, losing the current pregnancy through miscarriage as a result of amniocentesis/ CVS would be:

- ☐ 1 Extremely bad
☐ 2 Very bad
☐ 3 Neutral
☐ 4 Somewhat bad
☐ 5 Not at all bad
☐ 6 Don't know

7) If amniocentesis/ CVS was offered to me, I would have it. I am the type of person who wants every test available.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree
☐ 6 Don't know

8) For me, having an amniocentesis/ CVS would be:

- ☐ 1 Not at all frightening
☐ 2 Slightly frightening
☐ 3 Neutral
☐ 4 Quite frightening
☐ 5 Very frightening
☐ 6 Don't know

9) For me, giving birth to a child with a serious abnormality would be:

- ☐ 1 Very bad
☐ 2 Bad
☐ 3 Neutral
☐ 4 Good
☐ 5 Very good
☐ 6 Don't know

10) In my opinion, chromosomal disorders such as Down's syndrome would be the worst disability one could have.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree
☐ 6 Don't know

11) How likely do you think it is that you will have a baby with a serious abnormality?

- ☐ 1 Not at all likely
☐ 2 Less than likely
☐ 3 Neutral
☐ 4 Slightly likely
☐ 5 Very likely
☐ 6 Don't know

Section B continues on the next page 

[Section B continues here]

12) How strongly would you agree with the statement *"I feel I have the tools to make decisions that will influence my future"*?

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree
☐ 6 Don't know

13) How strongly would you agree with the statement *"I feel I can make a logical evaluation of the various options available to me in order to choose one of them"*?

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree
☐ 6 Don't know

14) How strongly would you agree with the statement *"I feel I can make decisions that will change my family's future"*?

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree
☐ 6 Don't know

SECTION C: OTHER 8 & AMNIOCENTESIS 818 / CVS

For the following statements please tick the box that best completes the phrase for you.

1) "If it is offered to me, I think my partner will want me to..."

- ☐ 1 Certainly decline amniocentesis/ CVS
☐ 2 Probably decline amniocentesis/ CVS
☐ 3 Not sure
☐ 4 Probably accept amniocentesis/ CVS
☐ 5 Certainly accept amniocentesis/ CVS
☐ 6 Not applicable

2) "I find my partner's opinion about accepting or declining the test..."


- ☐ 1 Not at all important
☐ 2 Less than important
☐ 3 Neutral
☐ 4 Quite important
☐ 5 Very important
☐ 6 Not applicable

3) "If it is offered to me, I think my midwife/obstetrician will want me to..."

- ☐ 1 Certainly decline amniocentesis/ CVS
☐ 2 Probably decline amniocentesis/ CVS
☐ 3 Not sure
☐ 4 Probably accept amniocentesis/ CVS
☐ 5 Certainly accept amniocentesis/ CVS

4) "I find my midwife's/obstetrician's opinion about accepting or declining the test..."

- ☐ 1 Not at all important
☐ 2 Less than important
☐ 3 Neutral
☐ 4 Quite important
☐ 5 Very important

Please turn over for Section D 

SECTION D: HOW YOU ARE FEELING

Read every sentence. Tick the box that best describes how you have been feeling during the LAST WEEK.

1) I feel tense or 'wound up':

- ☐ 3 Most of the time
☐ 2 A lot of the time
☐ 1 From time to time
☐ 0 Not at all

2) I get a sort of frightened feeling as if something awful is about to happen:

- ☐ 3 Very definitely and quite badly
☐ 2 Yes, but not too badly
☐ 1 A little, but it doesn't worry me
☐ 0 Not at all

3) Worrying thoughts go through my mind:

- ☐ 3 A great deal of the time
☐ 2 A lot of the time
☐ 1 From time to time, but not often
☐ 0 Only occasionally

4) I can sit at ease and feel relaxed:

- ☐ 3 Definitely
☐ 2 Usually
☐ 1 Not often
☐ 0 Not at all

5) I get a sort of frightened feeling like "butterflies" in the stomach:


- ☐ 0 Not at all
☐ 1 Occasionally
☐ 2 Quite often
☐ 3 Very often

6) I feel restless as I have to be on the move:

- ☐ 3 Very much indeed
☐ 2 Quite a lot
☐ 1 Not very much
☐ 0 Not at all

7) I get sudden feelings of panic:

- ☐ 3 Very often indeed
☐ 2 Quite often
☐ 1 Not very often
☐ 0 Not at all

Please turn over for Section E 

**SECTION E: ATTITUDES TO DOCTORS
AND MEDICINE**

Please tick the appropriate box to indicate how much you agree with each of the following statements

1) All doctors are good doctors.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree

2) I only consult a doctor if I'm at death's door.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree

3) Medicine is based on scientific principles.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree

4) Medicines can do as much harm as good.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree

5) The advice of doctors is mainly commonsense.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree

6) The improved health of the nation is due to effective medicine.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree

7) Doctors blame their patients if their treatment doesn't work.


- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree

8) I have absolute faith and confidence in all hospital doctors.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree

9) No two doctors will agree on what is wrong with a person.

- ☐ 1 Strongly disagree
☐ 2 Disagree
☐ 3 Neutral
☐ 4 Agree
☐ 5 Strongly agree

Section E continues on the next page 

[Section E continues here]

10) Medicine has cures for most diseases.

- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

11) Many medicines are just placebos or sugar pills.

- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

12) Often the only purpose of tests is to make the doctor feel less anxious.

- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

13) Medicine is the best profession a person can have.

- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

14) Doctors are too ready to solve patients' problems by prescribing tranquillisers.

- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

15) No matter how long you have to wait to see a doctor, it's worth it.

- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

16) Doctors know what's best for you.

- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

17) Doctors are important people in keeping us healthy.


- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

18) Most tests and investigations are done routinely rather than for a particular purpose.

- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

19) I don't like medical people.

- ☐1 Strongly disagree
- ☐2 Disagree
- ☐3 Neutral
- ☐4 Agree
- ☐5 Strongly agree

Please turn over for Section F 

SECTION F: BELIEFS ABOUT ILLNESS

Please tick the appropriate box to indicate how much you agree with each of the following statements

1) If I get ill, it is my own behaviour which determines how soon I will get well again.

- ☐ Strongly disagree
☐ Moderately disagree
☐ Slightly disagree
☐ Slightly agree
☐ Moderately agree
☐ Strongly agree

2) No matter what I do, if I am going to get sick, I will get sick.

- ☐ Strongly disagree
☐ Moderately disagree
☐ Slightly disagree
☐ Slightly agree
☐ Moderately agree
☐ Strongly agree

3) Having regular contact with my physician is the best way for me to avoid illness.

- ☐ Strongly disagree
☐ Moderately disagree
☐ Slightly disagree
☐ Slightly agree
☐ Moderately agree
☐ Strongly agree

4) Most things that affect my health happen to me by accident.

- ☐ Strongly disagree
☐ Moderately disagree
☐ Slightly disagree
☐ Slightly agree
☐ Moderately agree
☐ Strongly agree

5) Whenever I don't feel well, I should consult a medically trained professional.

- ☐ Strongly disagree
☐ Moderately disagree
☐ Slightly disagree
☐ Slightly agree
☐ Moderately agree
☐ Strongly agree

6) I am in control of my health.

- ☐ Strongly disagree
☐ Moderately disagree
☐ Slightly disagree
☐ Slightly agree
☐ Moderately agree
☐ Strongly agree

7) My family has a lot to do with my becoming sick or staying healthy.

- ☐ Strongly disagree
☐ Moderately disagree
☐ Slightly disagree
☐ Slightly agree
☐ Moderately agree
☐ Strongly agree

8) When I get sick, I am to blame.

- ☐ Strongly disagree
☐ Moderately disagree
☐ Slightly disagree
☐ Slightly agree
☐ Moderately agree
☐ Strongly agree

9) Luck plays a big part in determining how soon I will recover from an illness.

- ☐ Strongly disagree
☐ Moderately disagree
☐ Slightly disagree
☐ Slightly agree
☐ Moderately agree
☐ Strongly agree

[Section F continues here]

10) Health professionals control my health.

- ☐ Strongly disagree
- ☐ Moderately disagree
- ☐ Slightly disagree
- ☐ Slightly agree
- ☐ Moderately agree
- ☐ Strongly agree

11) My good health is largely a matter of good fortune.

- ☐ Strongly disagree
- ☐ Moderately disagree
- ☐ Slightly disagree
- ☐ Slightly agree
- ☐ Moderately agree
- ☐ Strongly agree

12) The main thing which affects my health is what I myself do.

- ☐ Strongly disagree
- ☐ Moderately disagree
- ☐ Slightly disagree
- ☐ Slightly agree
- ☐ Moderately agree
- ☐ Strongly agree

13) If I take care of myself, I can avoid illness.

- ☐ Strongly disagree
- ☐ Moderately disagree
- ☐ Slightly disagree
- ☐ Slightly agree
- ☐ Moderately agree
- ☐ Strongly agree

14) Whenever I recover from an illness, it's usually because other people (doctors, nurses, family, friends) have been taking good care of me.

- ☐ Strongly disagree
- ☐ Moderately disagree
- ☐ Slightly disagree
- ☐ Slightly agree
- ☐ Moderately agree
- ☐ Strongly agree

15) No matter what I do, I'm likely to get sick.

- ☐ Strongly disagree
- ☐ Moderately disagree
- ☐ Slightly disagree
- ☐ Slightly agree
- ☐ Moderately agree
- ☐ Strongly agree

16) If it's meant to be, I will stay healthy.

- ☐ Strongly disagree
- ☐ Moderately disagree
- ☐ Slightly disagree
- ☐ Slightly agree
- ☐ Moderately agree
- ☐ Strongly agree

17) If I take the right actions, I can stay healthy.

- ☐ Strongly disagree
- ☐ Moderately disagree
- ☐ Slightly disagree
- ☐ Slightly agree
- ☐ Moderately agree
- ☐ Strongly agree

18) Regarding my health, I can only do what my doctor tells me to do.

- ☐ Strongly disagree
- ☐ Moderately disagree
- ☐ Slightly disagree
- ☐ Slightly agree
- ☐ Moderately agree
- ☐ Strongly agree

SECTION G: YOU AND YOUR FAMILY

Please provide the following information by either filling out the spaces or crossing the appropriate box.

- 1) Age:
- 2) Ethnicity:
- 3) Religion:

<input type="checkbox"/> 1 Christian	<input type="checkbox"/> 2 Muslim
<input type="checkbox"/> 3 Hindu	<input type="checkbox"/> 4 Buddhist
<input type="checkbox"/> 5 Other: <input type="text"/>	
<input type="checkbox"/> 6 No religion	
- 4) Week of gestation:
- 5) Marital status:

<input type="checkbox"/> 1 Living together with partner, regardless whether married or not.
<input type="checkbox"/> 2 Used to live together with partner, but not anymore.
<input type="checkbox"/> 3 Currently in a relationship, but not living together.
<input type="checkbox"/> 4 Currently not in a relationship.
- 6) What is your highest educational qualification?

<input type="checkbox"/> 1 Primary School
<input type="checkbox"/> 2 Secondary School
<input type="checkbox"/> 3 University
<input type="checkbox"/> 4 Post-graduate studies
- 7) What is your occupation?
- 8) What is your partner's occupation?
- 9) Has anyone in your family been born with a genetic disorder such as Down syndrome?

<input type="checkbox"/> 1 Yes	<input type="checkbox"/> 2 No
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- 10) In your household, what is your annual income before taxes?

<input type="checkbox"/> 1 £0-35,000
<input type="checkbox"/> 2 £35,001-£150,000
<input type="checkbox"/> 3 Over £150,000
- 11) At the time you fell pregnant were you planning to do so?

<input type="checkbox"/> 1 Yes	<input type="checkbox"/> 2 No
--------------------------------	-------------------------------
- 12) How did you fall pregnant?

<input type="checkbox"/> 1 Naturally
<input type="checkbox"/> 2 Took fertility drugs
<input type="checkbox"/> 3 Had IVF
- 13) Aside your current pregnancy, do you have any children?

<input type="checkbox"/> 1 Yes	<input type="checkbox"/> 2 No
--------------------------------	-------------------------------
- 14) How many (biological) children do you have?
- 15) Have you ever had a miscarriage?

<input type="checkbox"/> 1 Yes	<input type="checkbox"/> 2 No
--------------------------------	-------------------------------
- 16) Have you ever had a termination of a pregnancy?

<input type="checkbox"/> 1 Yes	<input type="checkbox"/> 2 No
--------------------------------	-------------------------------
- 17) How difficult was it for you to get pregnant (this time)?

<input type="checkbox"/> 1 Very easy
<input type="checkbox"/> 2 Quite easy
<input type="checkbox"/> 3 Neutral
<input type="checkbox"/> 4 Quite difficult
<input type="checkbox"/> 5 Very difficult
- 18) Have you ever had an amniocentesis?

<input type="checkbox"/> 1 Yes	<input type="checkbox"/> 2 No
--------------------------------	-------------------------------
- 19) As far as you know, has anyone close to you (family or friend) ever had an amniocentesis?

<input type="checkbox"/> 1 Yes	<input type="checkbox"/> 2 No
--------------------------------	-------------------------------

20) Are you currently suffering from any of the following and have gone to see your doctor about the problem? Please tick the relevant box for each of the below:

- a. Diabetes ----- Yes ☐ No ☐
- b. Depression ----- Yes ☐ No ☐
- c. Asthma ----- Yes ☐ No ☐
- d. Schizophrenia ----- Yes ☐ No ☐
- e. Heart disease ----- Yes ☐ No ☐
- f. Migraine ----- Yes ☐ No ☐
- g. Hypertension ----- Yes ☐ No ☐
- h. Anxiety Disorders -- Yes ☐ No ☐
- i. Allergies ----- Yes ☐ No ☐
- j. Bipolar Disorder ---- Yes ☐ No ☐

21) Are you currently taking any medication? Yes ☐ No ☐

If 'Yes' please write down the names of all the medications that are you are taking below:

Thank you for completing this questionnaire. Please return this in the stamp addressed envelope or to one of the medical staff when you attend for your first visit.

6.2. **Appendix 2: Consent Form (pilot study)**

CONSENT FORM

Patient Identification Number (to be filled out by the researcher): _____

Title of project: *"Factors implicated in women's decision-making process regarding the uptake of amniocentesis/ CVS"*

Name of researcher: Marilena Tzafettas

Please tick the boxes:

1. I confirm that I have read and understand the information sheet dated for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
 2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
 3. I am aware that my medical records will be accessed strictly by my medical team. ☐
 4. I agree to take part in the above study. ☐
-

_____ (name of participant)	_____ (date)	_____ (signature)
_____ (name of person taking consent)	_____ (date)	_____ (signature)

6.3. Appendix 3: Information Sheet (pilot study)

Chief Investigator: Marilena Tzafettas
London Metropolitan University
Department of Psychology
166-220 Holloway Road
N7 8DB
E-mail: m.tzafettas@londonmet.ac.uk

PARTICIPANT INFORMATION SHEET

Study Title: Factors implicated in women's decision-making process regarding the uptake of amniocentesis/CVS

We would like to invite you to take part in a research study. Before you decide we would like you to understand why the research is being done and what it would involve for you, so please take the time to read the following information carefully. You may also wish to talk to others about the study, and please feel free to ask us if there is anything that is not clear to you or if you would like more information.

What is the purpose of the study?

The purpose of the study is to explore the different factors which may impact on a woman's decision to have an amniocentesis/CVS or not. Amniocentesis/CVS are similar tests that may or may not be offered to you depending on the results of your first trimester ultrasound scan (your doctor will give you more information about this procedure if considered appropriate). Past research has shown that when faced with such a decision a woman may be influenced by her own feelings and thoughts, and possibly by those of people she is close to. However, previous studies have not looked at a combination of these factors which will be the focus of this study. We understand that this is a very sensitive issue, and we are hoping that with your help we will be able to help women in the future decide whether or not they want to have an amniocentesis/CVS.

Why have I been invited to take part?

You have been invited to take part because you are above 18 years of age and have not yet had your 1st trimester screening ultrasound (11th-14th week of gestation), therefore meeting the criteria for the population under study. We are contacting **all** women in this stage of their pregnancy, who are under the care of King's College Hospital. Being asked to take part does not mean you are more likely to need amniocentesis/CVS.

Do I have to take part?

No, it is up to you to decide to join the study. If you agree to take part, you will be asked to sign a consent form. You are free to withdraw at any time, without giving a reason and this would not affect the standard of care you receive. If, at any point after handing in your questionnaire you decide that you do not wish to be included in the analysis of the study please contact the Chief Investigator at m.tzafettas@londonmet.ac.uk who will immediately remove and manually destroy your data.

What will happen to me if I take part and what will I have to do?

If you decide to take part in the study, you will be asked to fill out a questionnaire, which should take up to 30-40 minutes to complete. You will then be asked to return the completed questionnaire to the researcher, together with your signed consent form, using the enclosed pre-stamped envelope (or alternatively bring it with you to your scan appointment).

Please note that after completing the questionnaire your medical records will have to be accessed in order to determine whether you had an amniocentesis/CVS or not. This is essential for the outcome of this study and will strictly be done by members of your medical team who will maintain confidentiality and not disclose any personal information.

What are the possible disadvantages and risks of taking part?

This study addresses sensitive issues relating to pregnancy, and therefore carries the risk of causing feelings of distress. Information about relevant help-lines is provided on the debrief form so that you can access appropriate 24-hour support, but it is still very important for you to consider whether this is a sensitive topic for you, before deciding whether to participate or not.

What are the possible benefits of taking part?

We cannot promise that the study will help you, but we hope that it will offer you the opportunity to reflect on issues that might have not previously occurred to you in relation to your pregnancy and that this might help you in the decisions you may have to make regarding prenatal screening. In addition, we hope that the results of this study will contribute to a better understanding of the factors that mostly influence women in their decision to have an

amniocentesis/ CVS or not. This information may then be used by health professionals in order to support women in their decision.

What happens when the research study stops?

When the study is finished and we have analysed all the information, we aim to publish what we have found in relevant academic journals. We also hope to present the findings of the study at conferences but we will ensure that no individual participants in the study can be identified. You may also leave a contact e-mail address, if you wish to be informed of the results personally, although this will be a summary of the total results and not your individual score.

Version 4 – 29/01/2013

6.4. Appendix 4: Debrief Sheet (pilot study)

DEBRIEF SHEET

Thank you for taking part in this study which is part of my PhD in the area of Health Psychology at London Metropolitan University. The data from this study will be analysed to provide insight to the factors that may be implicated in women's decision making processes regarding the uptake of amniocentesis/CVS. Your personal details will not be included in this process. The researcher is only interested in group effects rather than data from a single individual.

By providing evidence for those particular factors which may influence women in the important decision of whether they should undergo amniocentesis/CVS, we can further inform health professionals who support women during their pregnancy especially in regard to making the decision to have an invasive test.

If you have any questions regarding this study please feel free to contact us at m.tzafettas@londonmet.ac.uk and we will be happy to answer any questions or receive any comments/feedback.

We would also like to take this opportunity to remind you that your responses are confidential and all results are published anonymously as group data. However, you still have the right to withdraw you responses, as your participation is completely voluntary. To do this, simply email us and we will be happy to remove your data.

If you would like to talk to someone or find out information about where you can receive help for any health related problems or concerns related to your pregnancy, the following registered agencies may be useful to you:

➤ **CareConfidential Helpline : 0800 028 2228**

CareConfidential Pregnancy Helpline offers a safe place to talk in confidence about any concerns you may have relating to pregnancy, or any difficulties you may be experiencing following an abortion, miscarriage, child loss or child separation.

➤ **The National Childbirth Trust – Pregnancy & Birth Line: 0300 330 0772**

Fully qualified antenatal teachers can answer all your questions relating to pregnancy or birth.

➤ **The National Childbirth Trust - Shared Experiences Helpline: 0300 330 0774**

This helpline is run by volunteers who have had challenging experiences of pregnancy, birth, and parenthood and can provide a listening ear and support for you.

If you have any specific concerns about your pregnancy we advise that you also speak to your GP, midwife or consultant.

Version 2 – 27/07/2012

6.5. Appendix 5: Voucher for prize draw

Kings College Hospital 
NHS Foundation Trust

£200 voucher to spend at Mothercare

For your chance to win a £200 voucher to spend at any Mothercare store simply complete the enclosed questionnaire IN FULL and return using the pre-stamped envelope. The winner will be randomly chosen electronically and will be notified via their preferred method as indicated below:

Please tick the box of your preferred method of contact & complete the relevant details:

☐ E-mail:

☐ Telephone:

IMPORTANT NOTE:

The information provided above will only be used by the Chief Investigator (Marilena Tzafettas) and only for the purposes of notifying you if you have won the £200 voucher. NO ONE ELSE will have access to these personal details.

You will only be entered into the prize draw if you return the questionnaire fully completed, so make sure you do not miss out any sections!

Version 1 – 29/01/2013

6.6. Appendix 6: Correlation Matrix

		The purpose of amniocentesis is to test for is the result of amniocentesis 100% reliable	Amniocentesis has a 1% chance of miscarriage	Follow-up options offered after diagnosing chromosomal disorder through amniocentesis	For me, having amniocentesis would be... (beneficial)	For me, from a physical point of view, having amniocentesis would be... (beneficial)	Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not (Jeans using)	For me, losing the current pregnancy through miscarriage as a result of amniocentesis would be... (severe)	If amniocentesis was offered to me I would have it because I am the type of person who wants every test	For me, giving birth to a child with a serious abnormality would be... (severe)	"I feel I have the tools to make decisions that will influence my future"	"I feel I can make a logical evaluation of the various options available to me in order to choose one of them"	"I feel I can make decisions that will change my family's future"	"It is offered to me, I think my partner will want me to..."	"I find my partner's opinion about accepting or declining the test..."	severely_reversed	nature_reversed	lightening_reversed	perceivedRisk_reversed
Correlation	The purpose of amniocentesis is to test for is the result of amniocentesis 100% reliable	1.000	0.000	0.331	0.000	0.176	0.240	0.000	0.153	0.000	0.067	0.000	0.233	0.000	0.000	0.000	0.000	0.000	0.000
	Amniocentesis has a 1% chance of miscarriage	0.331	-0.165	1.000	0.106	0.098	0.184	-0.081	0.067	0.000	-0.053	-0.000	-0.031	0.000	0.000	0.000	0.000	0.000	0.000
	Follow-up options offered after diagnosing chromosomal disorder through amniocentesis	0.000	0.700	0.106	1.000	0.115	0.062	0.297	0.053	-0.007	0.042	0.124	-0.178	0.071	0.068	0.072	0.208	0.067	0.288
	For me, having amniocentesis would be... (beneficial)	0.176	0.260	0.098	0.115	1.000	0.261	0.330	0.382	-0.177	0.231	-0.223	-0.096	-0.058	-0.160	0.413	-0.103	0.387	0.607
	For me, from a physical point of view, having amniocentesis would be...	0.240	0.061	0.184	0.062	0.261	1.000	0.217	0.305	-0.142	0.112	-0.132	-0.033	0.061	-0.084	0.018	-0.063	-0.058	0.256
	Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not	0.000	0.080	0.081	0.297	0.330	0.217	1.000	0.351	-0.196	0.392	-0.144	-0.044	-0.052	-0.006	0.282	-0.099	0.205	0.404
	For me, having amniocentesis would be... (severe)	0.153	0.143	-0.042	0.053	0.392	0.305	0.351	1.000	-0.182	0.339	-0.157	-0.028	0.107	0.08	0.487	-0.063	0.042	-0.238
	For me, losing the current pregnancy through miscarriage as a result of amniocentesis would be...	0.000	0.06	-0.036	-0.007	0.177	0.143	0.196	0.182	1.000	0.256	-0.216	0.044	0.068	-0.007	0.262	-0.436	0.333	0.218
	If amniocentesis was offered to me I would have it because I am the type of person who wants every test	-0.067	-0.026	-0.110	0.042	0.331	0.112	0.302	0.339	0.236	1.000	-0.236	0.040	-0.070	-0.151	0.480	-0.158	0.360	0.042
	For me, giving birth to a child with a serious abnormality would be...	0.000	0.06	-0.036	0.124	-0.223	-0.132	-0.144	-0.157	-0.216	-0.236	1.000	0.068	0.163	0.06	-0.324	0.117	-0.196	-0.108
	"I feel I have the tools to make decisions that will influence my future"	-0.031	-0.053	-0.060	-0.178	-0.096	-0.333	-0.044	-0.028	0.044	0.049	0.068	1.000	0.514	0.208	-0.087	-0.158	-0.150	-0.260
	"I feel I can make a logical evaluation of the various options available to me in order to choose one of them"	0.000	-0.000	-0.113	0.071	-0.058	0.081	-0.052	-0.107	0.069	-0.070	-0.163	0.514	1.000	0.822	0.034	-0.189	-0.093	
	"I feel I can make decisions that will change my family's future"	-0.233	-0.031	-0.097	0.068	-0.160	-0.284	-0.006	-0.138	-0.007	0.151	0.196	0.048	0.822	1.000	0.027	-0.062	-0.144	
	"It is offered to me, I think my partner will want me to..."	-0.160	0.087	-0.031	0.072	0.113	0.118	0.282	0.487	0.282	0.480	-0.324	-0.087	0.034	0.027	1.000	-0.251	0.417	
	"I find my partner's opinion about accepting or declining the test..."	0.000	0.00	0.114	0.08	-0.103	-0.081	-0.050	-0.083	-0.036	-0.158	-0.117	-0.168	-0.061	-0.251	1.000	-0.060	0.002	
	"I find my midwife's/obstetrician's opinion about accepting or declining the test..."	0.000	0.74	-0.136	0.067	0.387	-0.068	0.205	0.042	0.333	0.350	-0.196	-0.150	-0.003	-0.144	0.417	-0.060	1.000	
	severely_reversed	0.182	-0.18	0.326	0.286	-0.003	-0.120	-0.021	-0.341	0.082	-0.108	-0.263	-0.209	-0.187	0.03	0.02	0.13	1.000	
	nature_reversed	0.000	0.04	0.027	0.304	0.497	0.256	0.404	0.177	0.218	0.401	-0.361	-0.081	-0.101	0.052	0.10	-0.172	1.000	
	lightening_reversed	0.000	-0.04	0.018	0.036	0.297	0.302	0.110	0.281	0.168	0.258	-0.334	-0.054	-0.134	0.02	-0.164	-0.096	1.000	
	perceivedRisk_reversed	0.000	0.02	-0.189	-0.10	-0.04	0.02	0.022	-0.10	0.19	0.368	0.42	0.04	-0.04	-0.206	-0.181	-0.168	1.000	

6.7. Appendix 7: Oblique Rotation

Oblique Rotation	Component					
	1	2	3	4	5	6
I believe invasive diagnostic tests should never be done because they go against human nature	-0.831					
For me, having amniocentesis would be...(frightening)	-0.656					
"If it is offered to me, I think my partner will want me to..."	0.599		0.352			
"If it is offered to me I think my midwife/obstetrician will want me to..."	0.572					-0.326
"I feel I can make decisions that will change my family's future"		0.899				
"I feel I can make a logical evaluation of the various options available to me in order to choose one of them"		0.799				
"I feel I have the tools to make decisions that will influence my future"		0.786				-0.332
Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not			0.911			
For me, having amniocentesis would be...(reassuring)			0.766			
For me, having amniocentesis would be...(beneficial)			0.668			
"I find my midwife's/obstetrician's opinion about accepting or declining the test..."				0.791		
"I find my partner's opinion about accepting or declining the test..."				0.78		
For me, losing the current pregnancy through miscarriage as a result of amniocentesis would be...				-0.696		
In my opinion, chromosomal disorders such as DS would be the worst disability one could have					-0.86	
For me, giving birth to a child with a serious abnormality would be...					0.696	
The purpose of amniocentesis is to test for						0.86

Extraction Method: Principal Component Analysis.

Rotation Method: Oblimin with Kaiser Normalization.

a. Rotation converged in 14 iterations.

6.8. Appendix 8: Cronbach alpha SPSS output

Scale: Perceived behavioural control

Case Processing Summary			
		N	%
Cases	Valid	58	100.0
	Excluded ^a	0	0.0
	Total	58	100.0

a. Listwise deletion based on all variables in the procedure.

Reliability Statistics		
Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.804	.813	3

Item Statistics			
	Mean	Std. Deviation	N
"I feel I can make decisions that will change my family's future"	4.05	.804	58
"I feel I can make a logical evaluation of the various options available to me in order to choose one of them"	4.10	.831	58
"I feel I have the tools to make decisions that will influence my future"	4.00	1.026	58

Inter-Item Correlation Matrix			
	"I feel I can make decisions that will change my family's future"	"I feel I can make a logical evaluation of the various options available to me in order to choose one of them"	"I feel I have the tools to make decisions that will influence my future"
"I feel I can make decisions that will change my family's future"	1.000	.622	.638
"I feel I can make a logical evaluation of the various options available to me in order to choose one of them"	.622	1.000	.514
"I feel I have the tools to make decisions that will influence my future"	.638	.514	1.000

Item-Total Statistics					
	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
"I feel I can make decisions that will change my family's future"	8.10	2.621	.724	.524	.669
"I feel I can make a logical evaluation of the various options available to me in order to choose one of them"	8.05	2.752	.620	.410	.765
"I feel I have the tools to make decisions that will influence my future"	8.16	2.168	.639	.430	.767

Scale: attitude towards chromosomal abnormalities

Case Processing Summary

		N	%
Cases	Valid	58	100.0
	Excluded ^a	0	0.0
	Total	58	100.0

a. Listwise deletion based on all variables in the procedure.

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.466	.475	2

Item Statistics

	Mean	Std. Deviation	N
For me, giving burth to a child with a serious abnormality would be...	2.22	1.511	58
severity__reversed	3.88	1.215	58

Inter-Item Correlation Matrix

	For me, giving burth to a child with a serious abnormality would be...	severity__reversed
For me, giving burth to a child with a serious abnormality would be...	1.000	.311
severity__reversed	.311	1.000

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
For me, giving burth to a child with a serious abnormality would be...	3.88	1.476	.311	.097	
severity__reversed	2.22	2.282	.311	.097	

Scale: Benefits of amniocentesis/CVS

Case Processing Summary

		N	%
Cases	Valid	58	100.0
	Excluded ^a	0	0.0
	Total	58	100.0

a. Listwise deletion based on all variables in the procedure.

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.738	.743	3

Item Statistics

	Mean	Std. Deviation	N
Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not	3.81	1.572	58
For me, having amniocentesis would be...(reassuring)	3.97	1.228	58
For me, having amniocentesis would be...(beneficial)	3.90	1.597	58

Inter-Item Correlation Matrix

	Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not	For me, having amniocentesis would be...(reassuring)	For me, having amniocentesis would be...(beneficial)
Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not	1.000	.551	.530
For me, having amniocentesis would be...(reassuring)	.551	1.000	.392
For me, having amniocentesis would be...(beneficial)	.530	.392	1.000

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not	7.86	5.595	.644	.420	.549
For me, having amniocentesis would be...(reassuring)	7.71	7.685	.538	.317	.693
For me, having amniocentesis would be...(beneficial)	7.78	6.107	.532	.295	.697

6.9. Appendix 9: Cronbach alpha SPSS output (previously validate scales)

Scale: HADS - Anxiety scale

Case Processing Summary

		N	%
Cases	Valid	58	100.0
	Excluded ^a	0	0.0
	Total	58	100.0

a. Listwise deletion based on all variables in the procedure.

Reliability Statistics

	Cronbach's Alpha Based on Standardized Items	N of Items
Cronbach's Alpha	.577	7

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
I feel tense or 'wound up'...	6.45	5.866	.204	.179	.570
I get sort of a frightened feeling as if something awful is about to happen...	6.55	3.725	.691	.504	.334
Worrying thoughts go through my mind...	6.48	4.956	.449	.444	.481
I can sit at ease and feel relaxed...	5.36	7.954	-.414	.284	.734
I get a sort of a frightened feeling like "butterflies" in my stomach...	6.67	5.277	.414	.247	.501
I feel restless as I have to be on the move...	6.71	5.193	.328	.358	.527
I get sudden feelings of panic...	6.98	4.930	.527	.422	.458

Scale: Attitudes towards doctors & medicine

Case Processing Summary

		N	%
Cases	Valid	58	100.0
	Excluded ^a	0	0.0
	Total	58	100.0

a. Listwise deletion based on all variables in the procedure.

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.601	.619	19

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
All doctors are good doctors	48.55	31.760	.135	.533	.598
I only consult a doctor if I'm at death's door	49.05	32.190	.099	.408	.603
Medicine is based on scientific principles	47.31	32.323	.031	.377	.620
Medicine can do as much harm as good	47.76	32.397	.056	.339	.611
The advice of doctors is mainly commonsense	48.31	30.253	.256	.366	.580
The improved health of the nation is due to effective medicine	47.31	31.586	.161	.379	.594
Doctors blame their patients if their treatment doesn't work	48.90	28.691	.583	.736	.540
I have absolute faith and confidence in all hospital doctors	48.38	32.415	.067	.577	.608
No two doctors will agree on what is wrong with a person	48.60	28.770	.514	.727	.545
Medicine has cures for most diseases	47.90	29.007	.380	.378	.560
Many medicines are just placebos or sugar pills	48.98	30.614	.350	.644	.571
Often the only purpose of tests is to make the doctor feel less anxious	49.16	30.519	.340	.520	.571
Medicine is the best profession a person can have	48.38	29.889	.295	.472	.574
Doctors are too ready to solve patients' problems by prescribing tranquillisers	48.74	27.809	.522	.586	.536
No matter how long you have to wait to see a doctor, it's worth it	48.26	34.546	-.137	.407	.643
Doctors know what's best for you	47.72	31.993	.147	.666	.596
Doctors are important people in keeping us healthy	47.09	33.940	-.052	.271	.614
Most tests and navigations are done routinely rather than for a particular purpose	48.52	30.886	.261	.451	.581
I don't like medical people	49.40	32.138	.179	.595	.592

Scale: HLOC scale

Case Processing Summary

		N	%
Cases	Valid	56	96.6
	Excluded ^a	2	3.4
	Total	58	100.0

a. Listwise deletion based on all variables in the procedure.

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.563	.559	18

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
If I get ill, it is my own behaviour which determines how soon I will get well again	55.98	66.272	-.220	.279	.605
No matter what I do, if I am going to get sick, I will get sick	56.84	59.592	.111	.612	.563
Having regular contact with my physician is the best way for me to avoid illness	57.36	53.797	.491	.656	.502
Most things that affect my health happen to me by accident	57.02	58.672	.194	.350	.549
Whenever I don't feel well, I should consult a medically trained professional	57.25	55.500	.320	.572	.527
I am in control of my health	55.50	61.127	.023	.543	.579
My family have a lot to do with my becoming sick or staying healthy	56.77	55.091	.330	.459	.524
When I get sick, I am to blame	57.38	59.620	.106	.493	.564
Luck plays a big part in determining how soon I will recover from an illness	57.38	57.439	.242	.565	.541
Health professionals control my health	57.82	57.968	.272	.521	.538
My good health is largely a matter of good fortune	56.73	57.218	.190	.687	.550
The main thing which affects my health is what I myself do	55.61	57.406	.247	.619	.540
If I take care of myself, I can avoid illness	55.55	58.033	.203	.501	.547
Whenever I recover from an illness, it is usually because other people (doctors, nurses, family, friends) have been taking good care for me	56.32	56.186	.284	.473	.533
No matter what I do, I am likely to get sick	57.23	59.127	.139	.418	.558
If it is meant to be, I will stay healthy	56.77	53.745	.355	.521	.517
If I take the right actions, I can stay healthy	55.52	57.054	.247	.557	.540
Regarding my health, I can only do what my doctor tells me to do	57.29	62.608	-.035	.305	.586

6.10. Appendix 10: Amended Questionnaire (main study)

For the following statements please cross the box that best suits you.

OFFICE USE Date: _____
ONLY Patient ID: _____

SECTION A: HOW YOU ARE FEELING

Read every sentence. Tick the box that best describes how you have been feeling during the LAST WEEK.

- 1) I feel tense or 'wound up':
 - ☐ 1 Most of the time
 - ☐ 2 A lot of the time
 - ☐ 3 From time to time
 - ☐ 4 Not at all
- 2) I get a sort of frightened feeling as if something awful is about to happen:
 - ☐ 1 Very definitely and quite badly
 - ☐ 2 Yes, but not too badly
 - ☐ 3 A little, but it doesn't worry me
 - ☐ 4 Not at all
- 3) Worrying thoughts go through my mind:
 - ☐ 1 A great deal of the time
 - ☐ 2 A lot of the time
 - ☐ 3 From time to time, but not often
 - ☐ 4 Only occasionally
- 4) I can sit at ease and feel relaxed:
 - ☐ 1 Definitely
 - ☐ 2 Usually
 - ☐ 3 Not often
 - ☐ 4 Not at all
- 5) I get a sort of frightened feeling like "butterflies" in the stomach:
 - ☐ 1 Not at all
 - ☐ 2 Occasionally
 - ☐ 3 Quite often
 - ☐ 4 Very often
- 6) I feel restless as I have to be on the move:
 - ☐ 1 Very much indeed
 - ☐ 2 Quite a lot
 - ☐ 3 Not very much
 - ☐ 4 Not at all
- 7) I get sudden feelings of panic:
 - ☐ 1 Very often indeed
 - ☐ 2 Quite often
 - ☐ 3 Not very often
 - ☐ 4 Not at all

[End of Section A, Please continue to Section B]

SECTION B: ATTITUDES TO DOCTORS AND MEDICINE

Please tick the appropriate box to indicate how much you agree with each of the following statements

- 1) All doctors are good doctors
 - ☐ 1 Strongly disagree
 - ☐ 2 Disagree
 - ☐ 3 Neutral
 - ☐ 4 Agree
 - ☐ 5 Strongly agree
- 2) I only consult a doctor if I'm at death's door.
 - ☐ 1 Strongly disagree
 - ☐ 2 Disagree
 - ☐ 3 Neutral
 - ☐ 4 Agree
 - ☐ 5 Strongly agree
- 3) Medicine is based on scientific principles.
 - ☐ 1 Strongly disagree
 - ☐ 2 Disagree
 - ☐ 3 Neutral
 - ☐ 4 Agree
 - ☐ 5 Strongly agree
- 4) Medicines can do as much harm as good:
 - ☐ 1 Strongly disagree
 - ☐ 2 Disagree
 - ☐ 3 Neutral
 - ☐ 4 Agree
 - ☐ 5 Strongly agree
- 5) The advice of doctors is mainly common sense
 - ☐ 1 Strongly disagree
 - ☐ 2 Disagree
 - ☐ 3 Neutral
 - ☐ 4 Agree
 - ☐ 5 Strongly agree
- 6) The improved health of the nation is due to effective medicine.
 - ☐ 1 Strongly disagree
 - ☐ 2 Disagree
 - ☐ 3 Neutral
 - ☐ 4 Agree
 - ☐ 5 Strongly agree

[Section B continues on the next page]



[Section B continues here]

- 7) Doctors blame their patients if their treatment doesn't work.
- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
- 8) I have absolute faith and confidence in all hospital doctors
- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
- 9) No two doctors will agree on what is wrong with a person.
- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
- 10) Most tests and investigations are done routinely rather than for a particular purpose
- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
- 11) Doctors are too ready to solve patients' problems by prescribing tranquillisers:
- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
- 12) Often the only purpose of tests is to make the doctor feel less anxious.
- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree

13) Medicine is the best profession a person can have.

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree

14) Many medicines are just placebos or sugar pills

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree

15) No matter how long you have to wait to see a doctor, it's worth it.

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree

16) Doctors know what's best for you.

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree

17) Doctors are important people in keeping us healthy

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree

18) Medicine has cures for most diseases

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree

19) I don't like medical people

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree

[End of Section B, Please continue to Section C]



SECTION C: BELIEFS ABOUT ILLNESS

Please tick the appropriate box to indicate how much you agree with each of the following statements

- 1) If I get ill, it is my own behaviour which determines how soon I will get well again.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 2) No matter what I do, if I am going to get sick, I will get sick.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 3) Having regular contact with my physician is the best way for me to avoid illness.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 4) Most things that affect my health happen to me by accident.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 5) Whenever I don't feel well, I should consult a medically trained professional.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 6) When I get sick, I am to blame.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree

- 7) I am in control of my health.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 8) My family has a lot to do with my be-coming sick or staying healthy.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 9) Luck plays a big part in determining how soon I will recover from an illness.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 10) Health professionals control my health.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 11) My good health is largely a matter of good fortune.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree
- 12) The main thing which affects my health is what I myself do.
 - ☐ 1. Strongly disagree
 - ☐ 2. Moderately disagree
 - ☐ 3. Slightly disagree
 - ☐ 4. Slightly agree
 - ☐ 5. Moderately agree
 - ☐ 6. Strongly agree

[Section C continues on the next page.]



[Section C continues here]

13) If I take care of myself, I can avoid illness

- ☐ 1. Strongly disagree
☐ 2. Moderately disagree
☐ 3. Slightly disagree
☐ 4. Slightly agree
☐ 5. Moderately agree
☐ 6. Strongly agree

14) Whenever I recover from an illness, it's usually because other people (doctors, nurses, family, friends) have been taking good care of me.

- ☐ 1. Strongly disagree
☐ 2. Moderately disagree
☐ 3. Slightly disagree
☐ 4. Slightly agree
☐ 5. Moderately agree
☐ 6. Strongly agree

15) No matter what I do, I'm likely to get sick.

- ☐ 1. Strongly disagree
☐ 2. Moderately disagree
☐ 3. Slightly disagree
☐ 4. Slightly agree
☐ 5. Moderately agree
☐ 6. Strongly agree

16) If it's meant to be, I will stay healthy

- ☐ 1. Strongly disagree
☐ 2. Moderately disagree
☐ 3. Slightly disagree
☐ 4. Slightly agree
☐ 5. Moderately agree
☐ 6. Strongly agree

17) If I take the right actions, I can stay healthy

- ☐ 1. Strongly disagree
☐ 2. Moderately disagree
☐ 3. Slightly disagree
☐ 4. Slightly agree
☐ 5. Moderately agree
☐ 6. Strongly agree

18) Regarding my health, I can only do what my doctor tells me to do.

- ☐ 1. Strongly disagree
☐ 2. Moderately disagree
☐ 3. Slightly disagree
☐ 4. Slightly agree
☐ 5. Moderately agree
☐ 6. Strongly agree

[End of Section C, Please continue to Section D]

Version 4 - 05/02/2014

SECTION D: YOU & PRENATAL DIAGNOSTIC TESTS

For the following statements, please cross the box that best describes how you feel at the moment.

1) For me, having a prenatal diagnostic test would be:

- ☐ 1. Not at all beneficial
☐ 2. Less than beneficial
☐ 3. Neutral
☐ 4. Somewhat beneficial
☐ 5. Very beneficial
☐ 6. Don't know

2) Finding out whether my baby has a chromosomal disorder would give me the opportunity to choose whether I want to continue with this pregnancy or not:

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
☐ 6. Don't know

3) For me, having a prenatal diagnostic test would be:

- ☐ 1. Not at all reassuring
☐ 2. Less than reassuring
☐ 3. Neutral
☐ 4. Somewhat reassuring
☐ 5. Very reassuring
☐ 6. Don't know

4) For me, giving birth to a child with a serious abnormality would be:

- ☐ 1. Very bad
☐ 2. Bad
☐ 3. Neutral
☐ 4. Good
☐ 5. Very good
☐ 6. Don't know

5) In my opinion, chromosomal disorders such as Down's syndrome would be the worst disability one could have.

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
☐ 6. Don't know

[Section D continues on the next page]



6) How strongly would you agree with the statement "I feel I have the tools to make decisions that will influence my future"?

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
☐ 6. Don't know

7) How strongly would you agree with the statement "I feel I can make a logical evaluation of the various options available to me in order to choose one of them"?

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
☐ 6. Don't know

8) How strongly would you agree with the statement "I feel I can make decisions that will change my family's future"?

- ☐ 1. Strongly disagree
☐ 2. Disagree
☐ 3. Neutral
☐ 4. Agree
☐ 5. Strongly agree
☐ 6. Don't know

9) Please use the following space to note down the key reasons that led you to the decision to have the test you chose (CVS / amnio or Harmony):

SECTION E: ABOUT YOU

1) Are you currently suffering from any of the following and have gone to see your doctor about the problem? Please tick the relevant box for each of the below:

- | | | |
|----------------------|------------------------------|-----------------------------|
| a. Diabetes | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| b. Depression | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| c. Asthma | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| d. Schizophrenia | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| e. Heart disease | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| f. Migraine | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| g. Hypertension | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| h. Anxiety Disorders | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| i. Allergies | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| j. Bipolar Disorder | <input type="checkbox"/> Yes | <input type="checkbox"/> No |

2) Are you currently taking any medication?

- ☐ 1. Yes ☐ 2. No

3) If 'Yes' please write down the names of all the medications that are you are taking below:

End of the Questionnaire, Thank you!

6.11. Appendix 11: Information Sheet (main questionnaire study)

King's College Hospital 
NHS Foundation Trust

Chief Investigator: Marilena Tzafettas
London Metropolitan University
Department of Psychology
166-220 Holloway Road
N7 8DB
E-mail: m.tzafettas@londonmet.ac.uk

PARTICIPANT INFORMATION SHEET

Study Title: Factors implicated in women's decision-making regarding the uptake of prenatal diagnostic tests

We would like to invite you to take part in a research study. Before you decide we would like you to understand why the research is being done and what it would involve for you, so please take the time to read the following information carefully. You may also wish to talk to others about the study, and please feel free to ask us if there is anything that is not clear to you or if you would like more information.

What is the purpose of the study?

The purpose of this study is to explore the different factors which may impact on a woman's decision to have a prenatal diagnostic test or not. Diagnostic tests include the option of amnio / CVS or Harmony. Amniocentesis and CVS are tests that may have been offered to you if you were found to have an increased risk following your first trimester ultrasound scan (if not already, your doctor will give you more information about these procedures if considered relevant). Harmony is a blood test and you may have been offered this choice if you were found to be at moderate – high risk. Past research has shown that when faced with such a decision a woman may be influenced by her own feelings and thoughts, and possibly by those of people she is close to. However, previous studies have not looked at a combination of these factors which will be the focus of this study. We understand that this is a very sensitive issue, and we are hoping that with your help we will be able to help women in the future decide whether or not they want to have a prenatal diagnostic test and support them in making the right choice for them.

Why have I been invited to take part?

You have been invited to take part because you are above 18 years of age and have been offered the option of one of the above tests, therefore meeting the criteria for the population

under study. We are contacting all women in this stage of their pregnancy, who are under the care of King's College Hospital.

Do I have to take part?

No, it is up to you to decide to join the study. If you agree to take part, you will be asked to sign a consent form. You are free to withdraw at any time, without giving a reason and this would not affect the standard of care you receive. If, at any point after handing in your questionnaire you decide that you do not wish to be included in the analysis of the study please contact the Chief Investigator at m.tzafettas@londonmet.ac.uk who will immediately remove and manually destroy your data.

What will happen to me if I take part and what will I have to do?

If you decide to take part in the study, you will be asked to fill out a questionnaire, which should take up to 20 minutes to complete. You will then be asked to return the completed questionnaire to the researcher, together with your signed consent form, using the enclosed pre-stamped envelope.

What are the possible disadvantages and risks of taking part?

This study addresses sensitive issues relating to pregnancy, and therefore carries the risk of causing feelings of distress. Information about relevant help-lines is provided on the debrief form so that you can access appropriate 24-hour support, but it is still very important for you to consider whether this is a sensitive topic for you, before deciding whether to participate or not.

What are the possible benefits of taking part?

We cannot promise that the study will help you, but we hope that the results of this study will contribute to a better understanding of the factors that mostly influence women in their decision to have a prenatal diagnostic test or not. This information may then be used by health professionals in order to support women in their decision.

What happens when the research study stops?

When the study is finished and we have analysed all the information, we aim to publish what we have found in relevant academic journals. We also hope to present the findings of the study at conferences but we will ensure that no individual participants in the study can be identified. You may also leave a contact e-mail address, if you wish to be informed of the results personally, although this will be a summary of the total results and not your individual score.

What if there is a problem?

We think it is unlikely that anyone will be harmed by taking part in this study. However, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal London Metropolitan

University complaints mechanisms will be available to you. Please direct concerns to Dr Esther Murray, who will be supervising this project, at e.murray@londonmet.ac.uk

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. All questionnaires will remain anonymous, and will be kept separately from the consent forms so as not to be linked to individuals. All files will be safely stored in a place where no one outside the research team will have access, and will be destroyed after the end of the study.

Who is organising and funding the research?

The research is being carried out at King's College Hospital by Marilena Tzafettas, Dr Esther Murray, Dr Elizabeth Charman and Dr David Hardman of London Metropolitan University, and Professor Kypros Nicolaides of King's College. They have the responsibility for ensuring that this research study is conducted safely, ethically, and according to best practice has no financial interest.

Who has reviewed the study?

All research in the NHS is looked at by independent groups of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given a favourable opinion by the London – Stanmore National Research Ethics Service Committee.

Contact for Further Information

If you are interested in taking part in the study **please complete the consent form attached to this information sheet, and return it to the researcher together with the completed questionnaire** using the enclosed pre-stamped envelope. If you have any questions please feel free to contact the chief investigator, Marilena Tzafettas at m.tzafettas@londonmet.ac.uk . Alternatively you can contact the local principal investigator, Professor Kypros Nicolaides at kypros@fetalmedicine.com.

Thank you for taking the time to read this information sheet. Please find enclosed a box of "PregnaCare" vitamin and folic acid supplements which are yours to keep regardless of whether you decide to participate in the study or not.

Version 5 – 04/02/2014

6.12. **Appendix 12: Consent Form (main questionnaire study)**

CONSENT FORM

Patient Identification Number (to be filled out by the researcher): _____

Title of project: *"Factors implicated in women's decision-making regarding the uptake of prenatal diagnostic tests"*

Name of researcher: Marilena Tzafettas

Please tick the boxes:

1. I confirm that I have read and understand the information sheet dated for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.
3. I agree to take part in the above study.

(name of participant)

(date)

(signature)

(name of person taking consent)

(date)

(signature)

**PLEASE RETURN THIS SIGNED FORM TOGETHER WITH YOUR COMPLETED
QUESTIONNAIRE**

Version 3 – 04/02/2014

6.13. Appendix 13: Debrief Sheet (Main questionnaire study)

DEBRIEF SHEET

Thank you for taking part in this study which is part of my PhD in the area of Health Psychology at London Metropolitan University. The data from this study will be analysed to provide insight to the factors that may be implicated in women's decision making regarding the uptake of prenatal diagnostic tests. Your personal details will not be included in this process. I am only interested in group effects rather than data from a single individual.

By providing evidence for those particular factors which may influence women in the important decision of whether they should undergo a prenatal diagnostic test, we can further inform health professionals who support women during their pregnancy especially in regard to making the decision to have a prenatal diagnostic test.

If you have any questions regarding this study please feel free to contact me at m.tzafettas@londonmet.ac.uk and I will be happy to answer any questions or receive any comments/feedback.

I would also like to take this opportunity to remind you that your responses are confidential and all results are published anonymously as group data. However, you still have the right to withdraw your responses, as your participation is completely voluntary. To do this, simply email me and I will be happy to remove your data.

If you would like to talk to someone or find out information about where you can receive help for any health related problems or concerns related to your pregnancy, the following registered agencies may be useful to you:

Ø **CareConfidential Helpline : 0800 028 2228**

CareConfidential Pregnancy Helpline offers a safe place to talk in confidence about any concerns you may have relating to pregnancy, or any difficulties you may be experiencing following an abortion, miscarriage, child loss or child separation.

Version 3 – 04/02/2014

Ø **The National Childbirth Trust – Pregnancy & Birth Line: 0300 330 0772**

Fully qualified antenatal teachers can answer all your questions relating to pregnancy or birth.

Ø The National Childbirth Trust - Shared Experiences Helpline: 0300 330 0774

This helpline is run by volunteers who have had challenging experiences of pregnancy, birth, and parenthood and can provide a listening ear and support for you.

If you have any specific concerns about your pregnancy we I advise that you also speak to your GP, midwife or consultant.

Version 3 – 04/02/2014